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I. ON THE DISTRIBUTION OF THE CHOROIDAL ARTERIES AS A FACTOR IN THE LOCALISATION OF CERTAIN FORMS OF CHOROIDITIS AND RETINITIS.*

By E. NETTLESHIP.

Is there reason to think that the arrangement of the arteries in the choroid may affect the distribution of the changes in some forms of localised choroiditis and retinitis?

Two groups of cases are especially suitable for consideration in this respect, viz. :—(A) The whole family of central, usually senile, choroido-retinitis, not associated with any particular constitutional state; and (B) retinitis pigmentosa and cases of syphilitic retinitis accompanied by ring-scotoma.

In the family of central senile choroido-retinitis we can easily distinguish four well-marked clinical types though, as would be expected, mixed forms are met with. The types are (1) central guttate choroiditis, which is almost certainly the clinical equivalent of the so-called colloid nodules of the elastic lamina. This condition was first described by Mr. Hutchinson† in 1875, but has generally been called Tay's choroiditis at this hospital, from the conspicuous part ascribed

* The substance of this paper and the next formed the subjects of a Clinical Lecture given at the Moorfields Hospital on October 8th, 1902.

† R. L. O. H. Reports, vol. viii, p. 230, 1875. Goldzieher also wrote on similar cases before the publication of Fuchs's paper on Retinitis Circinata.

by Mr. Hutchinson in his paper to Mr. Waren Tay's observations and help. Some of the cases described in that paper showed other changes, but in nearly all of them the type of disease was that shown in Diagram 1,* taken from the Ophthalmological Society's Transactions, vol. iv, Pl. 2. In many cases the fovea itself is less affected than the perimacular region, a more or less complete belt of the spots encircling the disc and yellow-spot region, whilst the yellow-spot itself is comparatively free; but the yellow-spot is sometimes fully affected. Vision is damaged in various degrees, and since Tay's earlier observations were made many cases have been seen in which it was scarcely, if at all, lowered even when the actual macula was much involved: thus in the case from which Diagram I was taken V was 6/6 with each eye.

Type 2. An area of epithelial atrophy occupying the yellow-spot and more or less of the surrounding part. In well-marked cases the border is sharply defined, and shows a variety of irregularities, though the general shape is nearly circular or horizontally oval. (The diagram (No. 2) showing this form was taken from an original drawing.) There are varieties in which the shape is less regular, the border less defined, and the surface more pigmented. I do not know what morbid appearances precede the disturbance and removal of the pigment epithelium in this form of disease—perhaps hæmorrhage in some cases, superficial inflammation in others.

In Type 3 both the epithelium and choriocapillaris are destroyed, and the large vessels laid bare, these vessels themselves being usually much altered by opaque thickening of coats and contraction of lumen, and the blood-column in extreme cases either obliterated or hidden by the opacity of the coats. The diseased area is sharply defined, circular or oval in shape, and may be so large as to extend up to the disc. There is, in the typical cases, no collection of pigment.

* The references here, and further on, are to diagrams shown at the lecture.

(Diagram 3, showing this type, was taken from the Ophthalmological Society's Transactions, vol. iv, Pl. 8. There is also a good illustration in Jaeger's Large Atlas, second edition, Pl. 51.)

Type 4. In a fourth variety the corresponding part of the fundus is occupied by an oval or circular patch of densely opaque white, greyish-white, or yellowish-white substance lying beneath the retina and apparently upon the choroid. So far as I know, the origin and course of this form has not been worked out, nor is the structure of the patch known; the substance is, however, of appreciable thickness, as shown by ophthalmoscopic estimation and by the course of the retinal vessels. (The Diagram No. 4 of this form was from a drawing made by Mr. Holmes Spicer, and kindly lent by him.) Major Yarr* has lately published a drawing from a case that I think must have been an example of this deposit form of choroiditis, though he calls it choroidal atrophy; it shows, what is not uncommon in these cases, retinal vessels dipping into the mass and disappearing, doubtless anastomosing with vessels of the subjacent choroid. (Diagram 5 was copied from Yarr's plate.) The edge of the patch in Yarr's case is less regular than usual, but as, according to the history, it was of only about four months' duration, this is not surprising. Such a vascular communication† was shown also in two other diagrams taken from rough sketches of similar cases in my note-books (P. 12, 142, and P. 30, 37), and in one of these the patch of deposit was bordered by extravasated blood.

Another diagram was shown to illustrate the areolar form of atrophy (Type 3) emerging from a condition of previous deposit (Type 4), the deposit in the case from which this diagram was taken being in process of absorption instead of organising into dense tissue (P. 35, 52). That

* Yarr, Trans. Ophth. Soc., vol. xix, Pl. ix, Fig. 2.

† Retino-choroidal anastomoses occurring near the y. s. in cases of gross choroidal exudation were recorded by Loring in Knapp's Archives, vol. ii, 2, p. 1, in 1872.

such deposit may, on the other hand, be permanent is proved by a case published by Mr. Hartridge,* where a similar form of disease was watched for 14 years and seen to undergo little if any change.

In connection with these types of central choroiditis mention must be made of the retinitis circinata of Fuchs. It is ophthalmoscopically a disease of the deep retinal structures, and Ammann has found in microscopical sections blood between retina and choroid, and very marked disease of some of the neighbouring choroidal arteries; though he concludes that the hæmorrhages were derived from retinal vessels.†

My own experience is that, ophthalmoscopically, many mixed forms are found between typical retinitis circinata and one or other of the choroidal affections I have just alluded to. Even in Fuch's classical paper, his Fig. 7 (retinal) and Fig. 8 (choroidal) are from the two eyes of the same patient. I believe that even in typical cases of retinitis circinata the deeply-seated smoky-looking haze of the macular part of the retina is consistent with a disturbance of its choroidal nutrition, and that the later retinal appearances may be secondary.

I do not consider that the plate in Oeller's Atlas of Rare Ophthalmoscopic Conditions (C. Table I) with that of the earlier conditions of the same eye (C. Table VI) represent what Fuchs intends to convey by retinitis circinata, nor what most observers recognise as such, for the circinate arrangement here was preceded by obvious obliterative changes in the retinal arteries and coarse hæmorrhagic retinitis—conditions not seen, so far as I know, in what is usually recognised as the early stage of retinitis circinata.

The clinical course of the various types and their rela-

* Ophth. Soc.'s Trans., vol. xxi, p. 80, 1901.

† See Ammann, Knapp's Archives, vol. xxvii, p. 203, 1898 (from German edition, 1897). See also Goldzieher on his priority over Fuchs. Knapp's Archives, vol. xxviii, p. 638 (from German edition, vol. xxxiv, 1897).

tion to each other has not been fully investigated, and except Ammann's observations I know of no microscopical examinations. Observations of these various types of central change followed out from the commencement are much wanted but are difficult to get; the subjects seldom seek advice early, and often disappear when they find their sight getting no better; they are for the most part elderly, sometimes quite infirm; and again it often happens that the final details of the fundus changes as they proceed become more or less obscured by opacities in the lens. All the above forms of disease are, as implied in their nomenclature, usually confined to the centre of the fundus, but in all of them disease of the choroid is occasionally found elsewhere.

Has anyone watched the onset of Tay's guttate central choroiditis and seen it either increase or diminish? In one case where I found plenty of these spots in both eyes of a lady, aged 46, in 1886 (P. 12, 216), I believe I can say that the disease had spread over a somewhat wider area, and the individual spots become decidedly larger during the next 10 years; but I speak cautiously as to these points, because in the meantime the patient's lenses had become somewhat cloudy.

In regard both to Tay's disease and the three areolar types examination will, as already stated, lead to the frequent observation of intermediate and mixed forms and to the alliance of some of them with retinitis circinata; at least I feel sure we must not yet assume that the central areolar atrophy with thickening and narrowing of choroidal vessels (Type 3) is always atrophic from the beginning.* Some cases both of that and of the epithelial type may be simply atrophic, but it is more likely that in most of them a stage of exudation or inflammation precedes. Indeed, it is easy to understand that a similar disease of vessel-walls may,

* Ammann, in his paper on Retinitis Circinata, thinks the perivascular lymph-spaces may be primarily to blame in that disease. He is of course not speaking of the areolar choroidal atrophy, but the speculation may be extended to that form.

according to its degree or distribution, lead to mere atrophy in one case, but to œdema, hæmorrhage, and other changes, followed by atrophy or by organisation into new tissue, in another.

Why should the changes in this family group be so constantly limited to the area that includes the yellow-spot and optic disc? Probably the blood-supply has something to do with it, the blood-supply itself being related to the high structural and functional perfection of the retina at this part of the eye.

The capillary network both of the choroid and retina is much closer at the yellow-spot than in any other part. Whether the rapidity of the blood-stream through the close capillary mesh-work of the central area is as great as where the meshes are coarser, depends presumably on the dimensions and number of the respective arteries. In regard to the retina, Mr. Parsons* tells us that, relatively to the capillaries, the arterial supply for the central area is less than for other parts; if this be so a slight thickening of the coats of these arterioles would have serious consequences to the inner retinal layers. The corresponding part of the choroid, by which the outer layers of the retina are nourished, is well supplied by the short posterior ciliary arteries, though the great variability in their number as they penetrate the sclerotic may lead to variations in the effectiveness of the supply in different eyes. However this may be, we can hardly doubt that contraction of the lumen of one or more of the short ciliaries by endarteritis or other chronic change would soon tell on the integrity of the corresponding choroidal area; whilst if the chief inner or outer ciliary branch of the ophthalmic artery, from which the short ciliaries arise, were diseased, the area fed by all of its branches would of course be affected.

I suspect, therefore, that central senile choroido-retinal disease in its various manifestations is grounded chiefly upon disease of the posterior ciliary arteries—either the

* Parsons, *Ophthalmic Review*, vol. xx, p. 188. (July, 1901.)

trunk vessels or the branches that perforate the sclerotic near the optic nerve,—and that any affection of the retina itself is usually consequential. If this be so, we can readily understand why the disease is confined to the central area of the fundus. The process being non-infective, and conditioned by blood-vessels, differs radically from those kinds of choroiditis that are due to blood-state. In most cases of inflammation of the uveal coat and of the cornea due to a morbid blood-state the process tends to spread forward or backward to other parts, the amount of such extension being largely a question of the length of time that the malady remains active.

In so-called retinitis pigmentosa and in some cases of syphilitic retinitis the distribution of the disease is, I think, dependent in part on the arterial system of the choroid at the equatorial part of the globe.

In retinitis pigmentosa the ophthalmoscopic changes are often most conspicuous at, and sometimes confined to, the equatorial belt, ceasing not only behind it but in front also. In these cases the field shows a belt or portions of a belt of blindness between the seeing centre and the seeing periphery. In syphilitic retinitis, too, such a ring-scotoma or blind belt can not infrequently be found if sought for. (Diagrams were shown.)

It is impossible to explain this feature of these two diseases by anything in the structure of the choroid or retina. But it might be explicable if we could show that the supply of blood to the choroid was less efficient at the equator than either at the posterior or anterior parts of the fundus; and I think that this is the case. The posterior part of the choroid is supplied, and well supplied, by the short posterior ciliary arteries; the anterior part is supplied to a great extent by recurrent branches from the long posterior ciliary and anterior ciliary arteries. The terminal twigs of these anterior and posterior systems meet, and to a certain extent anastomose, at the equatorial region. The equator seems to

be a sort of "divide" between the two systems, and to be not very efficiently served by either, whilst the current must be slowed or reversed in many of the anastomosing twigs.

Given a congenital tendency (as in retinitis pigmentosa) to atrophy or hardening of the inner layers of the choroid, it would probably tell first where the nutrient stream was weakest; whilst if, owing to minor variations in the arterial arrangements just mentioned, some parts of the equator were better supplied than others, the incompleteness of the blind belt in certain cases would be explained. The explanation here suggested for the blind belt in the field in retinitis pigmentosa assumes that that disease takes its origin in the choroid, and this agrees I believe with the most recent views.

In order to explain the ring-scotoma of syphilitic retinitis by vascular supply, we must assume arteritis of the equatorial twigs of the choroidal arteries, either of the posterior or anterior system, or both; not on the whole a too strained assumption. Syphilitic retinitis is so very often accompanied by visible choroiditis, that even when at first no choroiditis can be proved by ophthalmoscopic examination, we may often safely prophecy that it will become visible later when the retina has cleared or become atrophic.

II. ON THE INFLUENCE OF OVER-USE AND FATIGUE OF THE EYES IN CAUSING ORGANIC DISEASE OF THE RETINA AND CHOROID.

(AFTER allusion to fatigue, of the eye-muscles from reading, writing and sewing, from fixed gazing, especially gazing upwards, and from rapid movements in following the objects passed in travelling; to the effects of evaporation, exposure and the friction of the eyelids, in producing troublesome mixed forms of asthenopia; and to iritis as often kept up or prevented from recovering, but seldom actually brought on, by overuse of the eyes; attention was particularly directed to the choroid and retina).

In regard to the choroid and retina the only case that, with our present knowledge, can be with certainty attributed to overuse is the "blinding" by Direct Sun-light, in which a small central scotoma follows immediately, or within a few hours, after looking at the sun without any, or with insufficient, protection. Good, though not quite perfect, recovery of vision usually follows after weeks or months, unless the primary lowering of visual acuity was very marked, but V. $\frac{1}{3}$ or less is seldom followed by satisfactory recovery.* The ophthalmoscope reveals either no visible changes or slight alterations of colour and clearness at the yellow spot, such as might be caused by œdema of retina and choroid and alteration in the quantity and distribution of the pigment granules of the retinal epithelium. In fact, experiments on the eyes of rabbits and frogs made under much severer exposure than can ever occur in the human eye, have shown that destruction of the rods and cones, exudation between retina and choroid and choroidal hæmorrhages are amongst the immediate results, whilst pigmented scar tissue may be a later product.†

* Mackay, *Ophthalmic Review*, vol. xiii, 1894, p. 92.

† Czerny and Deutschmann, according to Mackay, *loc. cit.*, p. 83.

The same cause, gazing at the sun, was believed to produce thrombosis of a branch of the retinal artery and other retinal and even choroidal changes, in a case published by Mr. Batten.*

Dr. Oliver, in 1897,† published a case in which choroido-retinal changes followed in both eyes after exposure to an extremely brilliant flash of lightning. In this case the R. eye was affected immediately or within a few hours, and showed marked fundus change nine days later; but the vision of the L. was unaffected till 10 days after the exposure, whilst fresh retinal hæmorrhage occurred in it nearly three months later. Though this young man's urine and heart were examined and found normal, I do not find any mention of syphilis in the record, and this omission much diminishes its value in the present connexion.

A case in which one eye became nearly blind with partial atrophy of the optic nerve, apparently from primary damage to the macular part of the retina, the other eye suffering for a time, but recovering with slight changes at the macula, was published by Mr. Treacher Collins‡ in 1896. The symptoms (central scotoma in each eye) in this case followed immediately after the patient (a woman aged 49) had stared at the sun, without protection, for five or ten minutes. It is noteworthy in this case that the failure of vision did not reach its worst till some days after the exposure, and also that the eye in which permanent, presumably ascending, damage occurred to the optic nerve, showed less visible change at the yellow spot than did the eye that recovered with a normal disc.§

A similar discrepancy between visual acuteness and ophthalmoscopic change in the two eyes was found in the case of a

* Rayner D. Batten, *Trans. Ophth. Soc.*, vol. xxi, 1901, p. 70.

† Oliver, *Trans. American Ophth. Soc.*, vol. vii, 1897, p. 613.

‡ Treacher Collins, *R.L.O.H. Reports*, vol. xiv, 1896, p. 374.

§ Compare O. Haab on *Secondary Atrophy of the Optic Nerves after Macular Disease*, *Abstract in Ophthalmic Review*, vol. xxi, Oct. 1902, p. 287.

Japanese gentleman whom I saw in 1898 (P. 48, 57). He was then 28, and told me that 10 years earlier he had damaged his eyes by looking for an hour at an eclipse of the sun without any protection. On the same day, almost immediately after, he found a "black patch" in front of whatever he looked at, but could see to each side of it. The next day his R. eye was covered up, and kept covered for several weeks, and it got perfectly well. The L., which remained open and in use, and entirely untreated until the R. was cured, never entirely recovered. When I saw him, 10 years after the accident, V. of the R. was $\frac{6}{5}$ with several ill-defined semi-confluent choroidal dots at or just below the fovea: V. of L. was only $\frac{6}{9}$, but I could see no changes at the y.s. or elsewhere; the defect was not optical.

It seems, therefore, as Mr. Rayner Batten has remarked in his paper already referred to, that the amount of damage to the retina varies much in these cases, and is not to be measured only by the length of time that the exposure lasts. We may add that the damage apparently does not depend entirely upon the absolute brightness of the sun-light or its spectral composition, for the two eyes often suffer in a different degree from an apparently equal exposure.

Such idiosyncrasy of the individual, or lower resisting power in one eye than in the other, is especially noteworthy, because we find cases that, as regards symptoms and ophthalmoscopic changes, are indistinguishable from the typical sun-blinding cases, but in which only moderate over-illumination, or none at all, can be alleged. It is, I think, most likely that fatigue of the central part of the retina either by relatively too intense light, or by too prolonged use in ordinary light combined with very accurate focussing, furnishes the true explanation in many cases of this group, the patient being perhaps rendered specially susceptible by general overwork or debility.

Some years ago I recorded* the case of a busy physician, aged 50, who noticed sudden failure of central vision with

* Ophthalmic Review, vol. vii, 1888, p. 33; Case III.

positive scotoma in his L. eye a few hours after using that eye at a microscope illuminated by direct sunlight. The eye very nearly, but never quite, recovered. There was an area of disturbance of the pigment epithelium at the y.s. In the same paper the case* of a naval officer is mentioned, in whose R. eye a permanent defect with metamorphopsia came on one day after this eye had been used for three hours continuously at the telescope of his theodolite in marine survey work. Two years later I found V. 6/9 barely, with a number of fine dots of choroidal or deep retinal disease at the y.s. The other eye, which he had never used for the theodolite work was perfect in every way. About the same time Dr. Brailey† recorded a case of a gentleman who had only one working eye, and it failed rapidly after he had been engaged closely at fine pen and ink drawing; fine central choroido-retinal changes were found.

In another case, perhaps less conclusive (P. 30, 19), a medical man, æt. 59, with two good eyes, each with about 2.5 D of My., undertook for a wager to count how many times the letter "e" occurred in a pamphlet of twelve pages of print, the type about equal to 5 Jäger. It was in the winter, was to be done against time, and he did it mostly by artificial light in the evening. Either during or immediately after this competition, he found his sight wrong, and discovered that the L. was defective. It got gradually worse, and remained so. When I saw him four years later, V. of this eye, corrected, was only 6/60; the central retina was occupied by a nearly complete zone of small bright white deposits with a few small dark blood dots at the y. s.; the retinal vessels, which showed no visible alteration, were in front of the deposits; a sort of retinitis circinata in fact. The other (R.) eye, with correction, saw 6/9, and showed no disease. The urine had been normal throughout the case.

I have notes of a considerable number of cases like those above mentioned, where a small positive scotoma, with or without noticeable metamorphopsia and fine changes at the y. s.,

* Case I.

† Brailey, Trans. Ophth. Soc., vol. vii, p. 177.

came on suddenly or quickly, but in which it could not be stated from the history that the eye or eyes had been either unduly worked or exposed to strong light. But in many such apparently causeless examples of acute central retino-choroiditis there may, as already suggested, have been relative overwork, or what is the same thing, lowered resisting power, owing to some condition of health or occupation.

It seems to me, therefore, that leaving the direct sunlight cases apart, we shall be wise to believe that prolonged use of the central part of the retina, especially for minute stationary objects, under strong illumination and with accurate focussing, can, in certain circumstances, cause organic disease of the retina or choroid or both, in the eye so used.

I believe also that fatigue or exhaustion of the retina and choroid sometimes causes, or at least contributes to, more severe and extensive disease than the form just described. In Case 5, in the paper just mentioned,* severe disseminated choroiditis, mostly central, came on immediately after exposure to glare, heat and wet in a young naval officer who was engaged all one night in combating a fire that broke out in his ship. His sight was much damaged. In Case 6, of the same paper, peripheral choroiditis with iritis and opacities in the vitreous occurred in a lad of 16 who had been doing heavy work out of doors, chiefly wood-sawing, in very hot, sunny weather in July; till then he had been at school; syphilis very improbable. In the next case,

(P. 18, 164).—A young lady of 19 or 20 suffered sudden failure of her L. eye after using a telescope, and soon after an attack of scarlet fever. She was told by an eminent ophthalmic surgeon that “effusion” was present; sight improved, but a cloud remained near the centre. At the age of 36, when pregnant, she was exhausted by having to nurse her father both day and night, and a miscarriage followed; the R. eye now failed rapidly, in one night, and she was told there was disease at the

* Ophthalmic Review, *loc. cit.*

back; the eye did not recover. Eleven years later, when 47, the L. (or first affected and now the only working eye) failed again; she had been sewing hard for hours one evening to finish some work for a bazaar, and found the dimness the next morning. I saw her a fortnight later (June 20, 1889), when 47 years old. In the L., V. was 6/60, and there were old choroidal changes and an obviously new focus of choroiditis, all in the central area. In the R. the changes were much more gross and extensive, and all old, and there were some iritic adhesions. She married at 24, and had nine children, all of whom lived, and one miscarriage.

(P. 19, 54).—An old lady went through much distress and strain at the age of 65, when her husband died, and at the same time her eyes broke down rapidly, so that after a few weeks she could neither read nor sew; no improvement took place. I saw her about nine months later, with very extensive superficial choroidal atrophy, chiefly central, but partly peripheral, and marked haze of the central retina. V. was only fingers at 1 to 3 metres.

A gentleman of 68 (P. 19, 24), suffering from general nervous exhaustion, underwent, in addition, a severe shock, and his sight failed rapidly in both eyes; he was told there was blood at the back. Ten months later I found much retinal hæmorrhage over the central area in both eyes, with some white patches in one. There was neither sugar nor albumen.

A lady, æt. 52 (P. 19, 192), with the cares of an establishment, added to permanent harass from the chronic nervous illness of her husband, went for a long drive one Saturday afternoon without a sun-shade, the sun shining directly on her face. That same evening she noticed a blur in reading, and found it was from the R. eye. I saw her three days later, March 28, 1893, and found a hæmorrhage and some white exudation in the retina up and out from the O.D., and just below the superior macular vessels. A fortnight later, the blood had gone, and the white patch was more sharply defined; later this quite disappeared, leaving the vein indented by an obviously thickened artery. Three years later (April, 1896), when she had one day been standing out in the sun directing some gardening operations, a similar attack occurred in the L. eye, and I found 6 days later a hæmorrhage and white effusion close to the lower-

outer edge of the O.D.; a month after this, almost complete absorption of blood and white effusion had taken place, and a vein at the centre of the blood area was seen to be crossed by an artery. Her physician considered her systemic arteries atheromatous and heart dilated, but always found the urine free from albumen. She was at one time liable to small extravasations, preceded by pricking pain, in the skin of the R. lower lid, and when I last saw her in 1899, she had had severe epistaxis. Her eyes were hypermetropic 4.5 D., but she began efficient glasses between 30 and 40. Once, when 30, she had gout in the foot, and had to give up beer.

In this case, exposure of the eyes to direct sun-light and heat produced on two occasions, we may suppose, general retinal congestion and rupture of a vein where it was crossed, and compressed, by a hard artery.

There is, I am sure, no doubt that in elderly myopic persons hæmorrhage, sometimes into the choroid, in other cases into the vitreous, is not uncommon as a result of combined overuse of the eyes and fatigue: the weakened vessel-walls of the myopic and senile choroid cannot bear the distension caused by excessive work or want of sleep. No doubt there may be contributory causes of congestion such as irregular eating and drinking, and carelessness as to the bowels, all of which are apt to occur at times of stress and exhaustion of whatever kind.

A spinster lady of 54 (P. 50, 106), much engaged in parish work, had had a specially hard winter with nursing and other work, and just before Easter she undertook a quantity of church and charity duty. On the Wednesday of Easter week her R. eye (with 14 D. of My.) failed, with black smuts. Two months later I found large webs in the vitreous and (old) choroidal changes at the y. s., besides a large annular staphyloma and marginal opacity in the lens; V. 6/36 with -14 D. The L., with My. 9 D. and V. 6/9, showed no changes anywhere except a narrow crescent.

A married lady, æt. 56 (P. 52, 85), was overwrought about the New Year, 1900, by the combined effects of influenza in her

house, a new cook who turned out a drunkard, and the death of an aunt. On January 12, 1900, she noticed a black thing before her R. eye, and on 19th (one week) I found large webs in the vitreous, but no other disease except a very moderate crescent V. with - 8 D. and a cylinder 6/18. The L., with 2 D. less of M., but similar As., had 6/9, and all normal. Such cases might easily be multiplied.

Several of my cases of choroidal and vitreous disease, associated with overuse, and others of the same kind without proved overuse, have been in plethoric, excitable, very active women with high myopia, and aged between 40 and 50. None were known to be alcoholic, and I am sure that most of them were not so, but now and then in such a case the suspicion has arisen. Similar cases are seen in men, but less commonly. The relative frequency in women is probably related to the menopause.

There seems no doubt that detachment of the retina may occur in similar circumstances, even in normally formed eyes, and we can scarcely doubt the causal influence of the excessive functioning.

A bank clerk, æt. 28 (P. 54, 26), had his sixth attack of influenza—a bad attack—at the end of January, 1900. The influenza pulled him down very much, but he had to return to duty before he was strong, and in addition to make up arrears of work. Soon after this he noticed something wrong with his sight, and discovered it to be in the R. eye, where detachment of the retina was found shortly afterwards. His eyes were emmetropic.

An actuary, æt. 57 (P. 55, 231), with My. 7 D. in the R. and 6 D. in the L., got detachment of the R. retina in April, 1901, after working hard at a statistical paper and correcting the proofs of it: he had not been accustomed to work requiring such a strain upon his eyes, and seems to have felt it a good deal. The eye had doubtless been a weak one, for Mr. Lawford had found a web in the vitreous when the patient had a troublesome cough some three years earlier, but this cleared up long before the detachment occurred.

In many of the examples just cited, the eyes were no doubt predisposed to degenerative lesions, as appears not only from the details of some of the cases themselves, but from the well-known occurrence of similar mishaps in the absence of marked fatigue or overuse. But in the particular instances quoted, there seems little doubt that the mischief would not have happened when it did, and would perhaps not have been so severe, had there been no fatigue or exhaustion.

And here I may say that I have gradually come to attribute greater influence to fatigue and overwork, local and general, than to more directly mechanical agencies in the production of intraocular hæmorrhage and even detachment of the retina. I, of course, do not say that stooping, straining, coughing, vomiting and other causes of temporary hindrance to the return of venous blood from the head; or muscular exertion causing violent action of the heart; or blows on the eye or concussion either of the head or the whole body, take no share in causing such maladies, but I think their influence has been over-rated, at any rate in the past, and that too little attention has been bestowed on physiological congestion from overuse.

ON THE CHILDREN OF PATIENTS WHO HAVE HAD
INTERSTITIAL KERATITIS.

By E. TREACHER COLLINS.

THE difficulty of obtaining absolute proof of the possibility of transmission of syphilis to the third generation was well demonstrated in an interesting paper by Dr. George Ogilvie, published in *The British Journal of Dermatology* in 1897. In it all the recorded evidence on the subject up to that date was critically examined. Dr. Ogilvie divided the subject into first, the possibility of the transmission of actual syphilis, and secondly, the production of a lowered state of vitality, "a dystrophic influence," "parasyphilis."

As regards the first, after having pointed out the difficulty of obtaining absolute proof on many points in connection with syphilis, upon which nearly all competent observers are agreed, he says, "In the same way we have to look upon the question of syphilitic transmission to the third generation. We have quoted above expressions of the two extreme opinions held on this subject. On the one hand we are told that 'there is not the slightest evidence' of such transmission; on the other, that 'there are undoubtedly cases' in which syphilis was transmitted. Both statements are equally unwarranted. The evidence before us furnishes us, if not with absolute proof, still with reasonable probability, that syphilis may descend to the third generation. On the other hand, there is no evidence to support the possibility of transmission to the fourth generation."

As to the second point, he sums up as follows:—"Without denying that the 'dystrophic' influence of syphilis may make itself felt in some way or other in the third generation, I consider that up to now statements to this effect are more or less vague conjectures, and incapable of being proved by clinical evidence. Nor do I see how we shall emerge

from this state of uncertainty, without that extensive co-operation of the general practitioner, which seems as unattainable as it would be of supreme value."

On these very important but undecided matters, it occurred to the writer that some data might be obtained, by collecting notes of the family histories of women, presenting themselves at an Ophthalmic Hospital suffering from interstitial keratitis, and having at least one other sign of congenital syphilis, who were married and had children.

There could be little doubt that these children would be the descendants of a grand-parent who had had primary syphilis; their number and condition of health could be ascertained, and some of them could be had up for examination.

To determine definitely whether or not the father of these children had had primary syphilis, would have been a matter of considerable difficulty, and it was decided not to attempt it.

So that the presence of syphilitic symptoms in the children themselves would not be proof of transmission to the third generation. The occurrence, however, of such symptoms in a number of the children from different families would be a very suggestive piece of evidence. On the other hand, the absence of syphilitic symptoms from the large majority of children from different families would definitely prove that women, the subjects of inherited syphilis, may have children perfectly free from any actual syphilitic taint.

The number of the woman's brothers and sisters living and dead could be noted, and a comparison could then be made as to the amount of mortality in the children of the two generations.

A comparison could also be effected as to the mortality of infants in the third generation, and the average mortality for children under one year of age given in the Registrar General's returns for the whole of London for some years past. This would afford some evidence as to the presence or absence of "dystrophic influence."

As the second decade in life is the one during which interstitial keratitis most frequently occurs, it necessarily took some time to collect a sufficient number of cases in which it appeared so late in life as to have allowed of the patients becoming mothers.

It was thought well to wait until twelve had been obtained, to render the data of sufficient value for publication.

The following twelve cases, the details of which have been arranged in tabular form, have all come under the writer's care as out patients at the Royal London Ophthalmic Hospital during the past six years.

Unfortunately, in the rush of out-patient work, in one or two cases some points have been omitted from the histories, and the patients have since passed away from observation.

The youngest of the twelve was 20 years of age, and the oldest was 52 years. It might naturally be questioned whether interstitial keratitis occurring as late as 52 could really be hereditary syphilitic in origin, and the writer would have hesitated in including this case, had not the eye affection been of the usual type, and the patient presented the most typically notched teeth.

In none of the cases has the presence of interstitial keratitis been relied upon alone as a diagnostic sign of inherited syphilis, in all except one there has been besides either, scars at the angles of the mouth, notched teeth, or a suggestive physiomy. In the one case in which none of these other symptoms were noted, the fact that the patient was one of a family of 15, 12 of whom died in infancy, has been taken as sufficient confirmatory evidence of the presence of inherited syphilis.

The 12 women have had 60 children and five miscarriages between them. Thirty-four of the children are living, and 26 have died. Of the 34 living, 25, of ages varying from 19 years to 4 months, are stated to be healthy and have had no symptoms of a syphilitic nature. Fourteen of these have been examined by the writer, and appeared in excellent health and free from all deformities.

Of the remaining nine which may be termed unhealthy—

One has had what was called “congestion of the brain”;

Five of one family are said to be frequently ill;

One has hydrocephalus;

One has had a rash on the skin, snuffles, ulceration about the anus, and lacrymal obstruction;

One of another family had snuffles in infancy.

Of the 26 that have died, 4 were still born; one died of measles aged 5 years, one of scarlet fever, age not stated, the remainder in infancy of such affections as “meningitis,” “diarrhœa,” “fits,” and one of small pox.

From the foregoing analysis, it would seem fair to assume that as 25 out of the 34 living children are presumably healthy, and 14 certainly so, women the subjects of inherited syphilis may certainly have healthy children free from all taint of that disease.

One of the living children seems to have presented definite syphilitic symptoms, and three of the others symptoms which may have been syphilitic in origin. Without any history of the presence or absence of primary syphilis in the father, this cannot be taken as proof of the transmission of syphilis to the third generation. On the other hand, the small proportion of the living children who have had symptoms of a syphilitic character, is presumptive evidence against transmission to the third generation.

It would be obviously impossible to get any accurate statement as to the number of miscarriages the patients' mothers have had. So that no comparison of any value can be made between the number of the patients' and their mothers' miscarriages.

It is worthy, however, of note that among these 12 women who were the subjects of inherited syphilis, though they had 60 children, a history of only five miscarriages could be elicited.

Coming next to compare the mortality amongst the children of the two generations:—

It is found that out of 91 children of the mothers' generation, 44 were stillborn, or died in early childhood, 48·3 per cent.

Out of 60 children in the next generation, 23 were still born, or died in early childhood, 38·2 per cent.

The Registrar General gives the average proportion of deaths in London under one year of age, for the ten years from 1890 to 1900, as 160 per 1,000, 16 per cent.

In the histories of several of the cases here recorded, the actual age at which the children died is not reported, it being often merely stated that they died in infancy.

It is found that in the mothers' generation, out of 91 children, 36 died under one year of age, or are said to have died in infancy, 39·4 per cent.

In the succeeding generation, out of 60 children, 22 died under one year of age, or are said to have died in infancy, 36·6 per cent.

From the above figures, it would seem fair to draw the following conclusions:—

That the mortality amongst the children of parents who have had primary syphilis is somewhat greater than amongst the grand children.

That, after some allowance is made for the probability of some of those stated to have died in infancy having been more than one year old, the difference between the average infant mortality in London (16 per cent.), and that amongst the grand children of those who had primary syphilis (36·6 per cent.), remains very marked, so marked as to make it impossible to avoid the inference of the presence of some "dystrophic influence."

The smallness of the number of miscarriages in the 12 women the subjects of inherited syphilis would seem to show that the dystrophic influence does not make itself felt upon the *fœtus in utero*.

I. No.	II. Name.	III. Age.	IV. Evidence of inherited syphilis.	V. Family history of patient.	VI. Children of patient.
1	Annie C. .. 26/8/97	27	R. E. interstitial keratitis. L. E. nebulæ of cornea. Scars at angles of mouth; upper lateral incisors and canines absent, other teeth good.	The 3rd of a family of 5, of whom 3 have died, 2 of "consumption," æt. 21 to 22 years; one died in infancy.	Two children, one dead, no miscarriages. 1st child, boy, æt. 3½ years; seen, well de- veloped and apparently healthy. Has had "congestion of brain," (? meningitis), was unconscious for about two days. Never any snuffles, said to have "breaking out on face at times." 2nd child, boy, died when 1½ years old from "meningitis."
2	Rebecca M.. 29/10/96	52	R. and L. eyes interstitial keratitis. R. inflamed 3 months; L. 3 weeks. Typically notched teeth.	One of three children, one brother living, a sister died at the age of 24 years.	Twelve children, 7 of whom have died in infancy. The five living are said to be frequently ill, nothing very definite concerning their illness known, none of them seen.
3	Clara G. .. 10/1/98	26	R. E. divergent and sight defective many years, a few white spots at macula V. = 6/24. L. E. interstitial keratitis. Teeth notched, of screw-driver shape. Later R. E. also became affected with interstitial keratitis.	One of a family of 11, eight of whom died in infancy, and three of whom are living.	Four children, one dead, no miscarriages. 1st child, æt. 7 years; seen, a healthy-look- ing child, no deformities, teeth good; never any illness; never any rash on skin or snuffles. 2nd child died at age of 1½ years of "diarrhœa." 3rd child, æt. 3 years; seen, a healthy-look- ing child, no deformities; never any illness; never any rash on skin or snuffles. 4th child, æt. 10 months, also seen, healthy, and no history of any illness.

I. No.	II. Name.	III. Age.	IV. Evidence of inherited syphilis.	V. Family history of patient.	VI. Children of patient.
4	Mary G. .. 5/12/98	38	R. E. interstitial keratitis.	One of a family of 15, twelve of whom died in infancy. Two sisters and one brother living, patient the youngest.	Fourteen children, 11 dead, 2 miscarriages. One died, æt. 5 years, of measles, two were stillborn, eight were born alive but died in infancy, some from "fits." The three living are æt. 19, 18, and 4 years respectively. The one æt. 4 seen, apparently quite healthy and well formed; the other two stated to have good health.
5	Mrs. F. .. 11/5/99	23	L. E. shrunken 14 years. R. E. interstitial keratitis. Physionomy and central incisor teeth suggestive of inherited syphilis.	One of a family of 4, one sister living; one brother and one sister died in infancy.	One child, no miscarriages. Child æt. 3 years, seen, healthy-looking and well developed, has never had any rash on skin or snuffles.
6	Laura J. .. 26/6/99	27	Interstitial keratitis both eyes. L. first inflamed 2 years ago. R. four months ago. Physionomy and teeth typical of hereditary syphilis.		Four children, 2 dead (stillborn). Eldest living, æt. 4 years, seen; head hydrocephalic, never any fits; the younger æt. 1- $\frac{1}{2}$ years.

7	Emily D. .. 17/7/99	33	Interstitial keratitis both eyes. Scars at angles of mouth. Nothing typical about teeth or physiognomy.	One of a family of 15, seven of whom are living; the others mostly died in infancy.	Five children, all living; "all healthy," no history of snuffles or rash on skin in in- fancy in any of them. The 2nd, æt. 10 years, seen; also the youngest, both in good health, no deforma- ties, teeth good. The youngest has phy- ctenular ophthalmia.
8	Mrs. P. .. 15/3/00	25	Signs of past interstitial kera- titis in both eyes. Inflammation in them first four years ago, and again one year ago. Scars at angles of mouth. No deafness. Teeth not notched.	The 7th of a family of 10, six of whom are living. Her mother had 4 mis- carriages before patient was born. The first four children are said to have died of smallpox, pneumonia, or violence. The 8th child is nearly blind with one eye.	Four children, 1 dead. 1st child died when 3 weeks old of smallpox. 2nd child, for, æt. 5 years, had snuffles from birth till the age of 6 months; had a rash on the face and arms at age of 3 weeks, lasting about a week; pneumonia at the age of 2 years, and also ulceration about arms. Child seen; has lacrymal obstruction on the left side, eye said always to have been watery. No probe could be passed, bony obstruction, otherwise the child appears healthy. 3rd child, boy, æt. 4 years, seen; fairly healthy, no deformities, never any snuffles, rash on skin or sores on body. 4th child, æt. 4 months, seen; fairly healthy, never any snuffles or rash on skin.
9	Eliz. W. .. 31/5/00	20	L. E. interstitial keratitis. Physiognomy suggestive of in- herited syphilis. Scars at angles of mouth. Teeth not notched.	The eldest living of a family of 8. Three died in infancy.	One child, æt. 11 months, seen; apparently in excellent health, no deformities, never any rash on skin or snuffles.

I. No.	II. Name.	III. Age.	IV. Evidence of inherited syphilis.	V. Family history of patient.	VI. Children of patient.
10	Jane D. .. 9/7/00	39	L. E. interstitial keratitis. Scars at angles of mouth.	One of a family of about 7. Two brothers and one sister living. Three or more died in infancy.	Eight children; 2 dead; 3 miscarriages. One died of scarlet fever; the other, "born blind," died, æt. 8 months. Eldest living is 19 years of age. One, æt. 3 years, seen; in good health, well de- veloped. None of the children have had snuffles or rash on the skin at birth.
11	Milly B. .. 25/4/01	26	Interstitial keratitis in both eyes. R. E. affected three years ago. L. E. 18 months ago. Scars at angles of mouth. Teeth not notched.	One of a family of 10. Three died in infancy, seven are living.	Three children, one born at 6 months, and died on second day. Eldest living is æt. 4 years, said to have had snuffles when a baby, no rash on skin at any time. Youngest, æt. 15 months. Both children seen; strong, well formed, and healthy- looking.
12	Lilly A. .. 29/3/02	26	R. E. inflamed 5 years ago, nebulae of cornea. L. E. affected 5 weeks, inter- stitial keratitis. Scars at angles of mouth. Upper central incisors wedge- shaped, and one notched, lateral incisors absent. Physiognomy suggestive of inherited syphilis. No deaf- ness.	The second of a family of three, all living.	Two children, both living; no miscarriages. Eldest child, æt. 3 years, has had no illness except measles. Youngest, æt. 14 months, never any illness. Both children seen in good health, and no deformities.

THE HEALING OF WOUNDS OF THE RETINA, CHOROID, AND
SCLERA, WITH SOME REMARKS ON THE PATHOLOGY
OF "RETINITIS PROLIFERANS."

By J. HERBERT PARSONS, *Curator*.

THE material upon which this research is based consists of experimental lesions produced in six monkeys, and three cases of injury by foreign bodies, in each case a piece of steel, which perforated the globe and led to excision. The latter are selected from a large number of such excised eyes which have been examined in the Pathological Laboratory of the Royal London Ophthalmic Hospital. Many of these are useless for my purpose, being hopelessly disorganised; but many others show similar changes to those found in the three recorded, the latter being chosen because they present a well-marked gradation, and further, emphasise the main causes of otherwise conflicting results.

I propose, first, to review the rather scanty literature upon the subject. A vast amount of work has been done upon corneal wounds, but wounds of the other coats of the eye have received but meagre attention. This is the more remarkable in that the conditions present in the eye afford, in many ways, a very specially favourable field for settling some moot points in general pathology, apart from their specific interest to ophthalmologists. This fact has been fully recognised in dealing with the cornea and anterior chamber, the latter, of course, particularly from the bacteriological point of view. It is none the less patent in dealing with the sclera, choroid, retina and vitreous, all of which present special characteristics which enable us to exclude various contingencies which vitiate experiments upon other parts of the body.

Secondly, I propose to describe in detail the actual lesions produced in the experiments upon monkeys, and the

clinical and pathological notes of the lesions produced by accident in man.

Finally, I shall gather together, discuss and criticise the data obtained, adding a few remarks showing the bearing of some of the results upon the pathology of so-called "retinitis proliferans."

HISTORICAL.

As regards wounds of the *retina*, only one monograph of importance has been published. Doubtless many facts of importance are published incidently in the records of the pathological lesions occurring in human eyes, but these are invariably so vitiated by concomitant factors that they possess little importance unless controlled by experimental results. The same criticism would, of course, apply to the three pathological cases reported in this paper, were they not controlled by the experimental investigations.

The paper referred to is one by Tepljaschin,⁽¹⁾ of Kasan, published in 1894, on "The Histological Changes in the Retina after experimental Injury." This is an exhaustive paper on the subject, and some of the deductions drawn by the author from his preparations are so at variance with current pathological ideas, and my own conclusions, that it requires somewhat detailed consideration.

The experiments were made upon rabbits, "not less than 50 experiments" having been performed. An attempt was made to wound the retina without injuring the choroid and sclera: it is improbable that this was effected in many, if any, of the cases. A discission needle was passed through the coats of the globe 5—6 mm. behind the margin of the cornea, and a linear wound made in the retina on the opposite side. Perforating wounds were also examined, made by a Beer or Graefe knife inserted 4 mm. behind the corneal margin, a meridional section of 4—5 mm. being made. Finally, in other cases the retina was cauterised, as in the experiments of Roth⁽²⁾ and Baquis,⁽³⁾ by an electro-cautery thrust into the globe as far as possible behind the limbus.

The animals were chloroformed to death at intervals after the operation varying from 22 hours to 285 days. For vertical sections of the retina, the tissue was fixed in Flemming's weak or strong osmic-chromic-acetic mixture, and cut in celloidin. Flat preparations were stained by a modification of Ehrlich's *intra vitam* methylene blue method.

Perforating wounds, and those produced by cauterisation cause an increase of the wandering cells in the vitreous, commencing on the 2nd day and reaching a maximum on the 4th or 5th. This is most marked in the immediate vicinity of the wound, but extends for varying depths into the vitreous. Are these cells entirely due to emigration from the surrounding blood-vessels, or are they, at least in part, due to division of the normal wandering cells of the vitreous? H. Pagenstecher,⁽⁴⁾ from experiments in which a foreign body was introduced into the vitreous, agrees with the majority of authors in regarding them as due to emigration. Hebb and Brailey,⁽⁵⁾ on the other hand, in a paper on "Suppurative Hyalitis," "deduce the general conclusion that the migration of the colourless blood-corpuscles bears no part in these cases of suppuration of the vitreous body." Haensell,⁽⁶⁾ from experimental data, holds the intermediate position regarding the increase to emigration from the retinal and choroidal vessels, supplemented by proliferation of the normal cells found in the vitreous. Potjechin⁽⁷⁾ ascribes the primary increase to emigration, and subsequent increase on stronger or longer inflammation to proliferation. Wedl and Bock⁽⁸⁾ figure vitreous cells in different stages of direct cell-division, and the possibility of simple cell-division in leucocytes is proved by the researches of Bizzozzero, Ranvier, Klein, Stricker, Flemming, Lawdowsky and others. That they can also increase by karyokinesis is shown by Peremeschko, Kultschizky, Marchand, Metschnikow, Schpronk and Flemming. Further, Arnold describes increase of leucocytes by so-called "fragmentation" (an appearance similar, if not identical, with that of the ordinary polymorphonuclear cell). Tepljaschin figures examples of each

mode of cell-division, from leucocytes found in the vitreous on the 4th day after operation.

Regressive metamorphoses occur in some cells even on the 1st day after operation, and these become more and more patent as time goes on, so that after the 4th or 5th day, when the leucocytes tend to decrease in numbers, they become predominant. The cells now show nuclei with deeply stained (with safranin) granules of varying shape and size, or the nuclei are broken up into small deeply stained particles. These are doubtless forms of nuclear *débris* from dead leucocytes (karyorhexis, karyolysis). Other cells show vacuoles; others again, fatty degeneration.

From the 4th to 5th day some of the leucocytes become grouped around new formed fibrous tissue, which fills the perforating wound. Karyokinetic figures are seen amongst these.

Sooner or later the inner surface of the retina (internal limiting membrane) becomes covered with flattened cells with well-marked oval nuclei. These are endothelial cells; "in flat preparations, stained with methylene blue, they are seen to be derived from wandering cells." (Tepljaschin). This appearance is familiar in pathological human eyes in many conditions, *e.g.*, chronic retinitis (Iwanoff),⁽⁹⁾ shrunken vitreous (Duke Carl Theodor)⁽¹⁰⁾, detached retina (Norden-son),⁽¹¹⁾ intraocular cysticercus (Dolina),⁽¹²⁾ &c.

In later stages, a lamina of connective tissue often forms over the inner surface of the retina, "which is so intimately bound up with the retina, that the radial supporting fibres of the latter (*i.e.*, Müller's fibres) pass over into this lamina and take part in its formation." (Tepljaschin.) Similar structures are also seen in pathological human eyes, where they are known as *retinitis proliferans* (Manz),⁽¹³⁾ due, according to Leber,⁽¹⁴⁾ to hæmorrhages. The question arises, can these fibrous tissue developments arise from wandering cells, or are the elements of other tissues necessary to their formation?

Much controversy has taken place in the realm of general

pathology as to this question, and, whilst the transition of leucocytes into granulation tissue was formerly admitted, much doubt has been cast upon it in recent years, dating especially from the opinions expressed by Ziegler, Marchand, Grawitz, and others at the 10th International Medical Congress in Berlin, in 1890. (Sherrington and Ballance* in the previous year published an important paper in which they practically proved that the new fibrous tissue cells do not arise from leucocytes, but from plasma cells which invade the injured area immediately after the leucocytic invasion. These plasma cells or fibroblasts are derived from those normally present in mesoblastic connective tissues. The method used was the examination of the films of tissue invading the space (1/20 mm. thick) between two cover-glasses, which had been embedded in the subcutaneous tissue of living rabbits or guinea-pigs for varying lengths of time from 4 hours to 18 days.)

As regards the eye, H. Pagenstecher's experiments were considered by him to confirm the then accepted view. Tepljaschin, using the methylene-blue method, lays great stress upon the fact that the leucocytes take up this stain, whilst the embryonic connective tissue cells do not. Many of the former are seen to arrange themselves in layers and become elongated, spindle or star-shaped. They thus approximate the form of new fibrous tissue cells. The same phenomenon was found to occur in a case of cyclitis; hence he concludes that "wandering cells of the vitreous can, in the latest stages after injury of the eye, and also under the influence of chronic inflammatory processes in the uveal tract, become transformed into fixed cell-elements."

The behaviour in the blood-vessels is next considered. In the rabbit, the large retinal blood-vessels lie on the inner side of the internal limiting membrane, the capillary vessels passing through it but penetrating only into the nerve-fibre layer (Krause). Injury of the larger vessels was avoided in the experiments. A few days after the operation,

* Sherrington and Ballance, *Jour. of Physiology*, vol. x, 1889, p. 550.

proliferation of the endothelium of the capillaries by indirect division was observed. In later stages, large, flat, monoclear cells, with long thin processes, were seen in the immediate neighbourhood of the vessels, apparently directly connected with their walls. Such cells are unknown in normal adult rabbits, but are found in fishes and frogs (Hans Virchow, Zimmerman), and also in the embryo (R. Virchow, Kölliker, Lieberkuhn). From flat preparations, stained with methylene-blue, Tepljaschin concludes that we have here "so-called vessel-forming cells and especially an intracellular process of new vessel-formation, like that described in embryonic development and in inflammatory processes by Ranvier, Ziegler, &c." New vessels were not formed in the vitreous except in the case of the masses of granulation tissue filling perforating wounds.

In the early stages, general retinal oedema was seen, most marked around the ganglion cells and the outer cells of the inner nuclear layer. This was seldom observed three or four weeks after operation, and was absent after one to two months.

In the nerve-fibre layer many varicose nerve-fibres were found, like those described by H. Müller⁽¹⁵⁾ as characteristic of albuminuric retinitis, but since discovered in other conditions. They have been investigated by Roth and Baquis. They are found from 22 hours after injury, and occur both peripherally and centrally to the wound, but earlier centrally the nearer the wound to the papilla. On the peripheral side of the wound they occur later than on the central side, and they also appear later the nearer the wound to the papilla. The cut ends of the nerve-fibres swell up on the central side, but this does not occur so much upon the peripheral side; hence the former are globular, the latter club-shaped. Various hypotheses have been advanced to account for the varicose condition, such as sclerosis of the nerve fibres (Virchow), hyaline degeneration (Recklinghausen), hypertrophy of the nerve-fibres (H. Müller), hæmorrhage due to albuminuria (Berlin), post-mortem changes (Dogiel), &c.

(Virchow's view is probably the correct one : the phenomenon may even be due to an extremely fine myelin sheath, such as is known to be present on some nerve fibres formerly described as non-medullated. It is likely that a naked axis cylinder does not exist, except perhaps in the small ramifications at the terminal synapse. If this view be correct, the varicosity would be anticipated by analogy with other degenerating medullated fibres. The early onset of varicosity on the peripheral side when the injury is near the ganglion cell from which the axon springs is probably due to shock to the cell, and is analogous to the presence of Marchi degeneration in the central ends of certain motor nerves, *e.g.*, hypoglossal, when the nerve is forcibly torn out, a result which does not follow if the nerve is merely cut through. The shock to the cell is apparently always sufficient in the case of retinal injury to lead to ultimate degeneration of the part still attached to the ganglion cell, but is less when the wound is near the papilla, and therefore presumably farther from the cell. This extreme susceptibility of the retinal ganglion cells may also possibly account for the optic atrophy in cases of injury to the optic nerve in the optic foramen, &c. (*e.g.*, cases of fractured base), a degeneration which is difficult to reconcile with the general Wallerian law. At the same time the presence of efferent fibres in the optic nerve must be taken into account, and also the possibility that they are more numerous than has been hitherto suspected*). No regeneration of nerve fibres was observed, although the club-shaped extremity of the part united to the cell of origin is indicative of continued, if lowered, vitality. (Such a result was to be expected. The axons of the ganglion cells are analogous to true intraspinal axons, and on no reasonable hypothesis to spinal dorsal root fibres, as has sometimes been stated. These

* See my paper on Degenerations following Lesions of the Retina, Brain, vol. xxv, 1902. These questions are discussed here because they require special methods for their elucidation, and they do not come within the immediate purview of this paper.

latter are represented by intra-retinal fibres,—either those of the inner nuclear layer, or those of the outer nuclear layer, but *which* it is difficult to say.* The ganglion cell fibres belong, therefore, strictly speaking, to the central nervous system, and such, as is well known, never regenerate). In preparations fixed by Flemming's solution, black droplets were observed amongst the fibres, due to broken up myelin. (These doubtless represented some medullated fibres, which occur in abundance in the rabbit's retina. They cannot, therefore, be regarded as evidence of a fine myelin sheath to so-called "non-medullated fibres.") Leucocytes were observed in large numbers around the degenerating fibres, distinguished from fixed cells by the fact that they stained with methylene blue. In late stages (194 days) ganglion cells are found only near the ora serrata on the peripheral side of the wound, whilst, still later (285 days), both ganglion cells and nerve fibres had entirely disappeared peripherally. In both these cases the nerve cells of the inner nuclear layer were intact, though they formed a thinner layer, due probably to the atrophy of the ganglion cell processes.

In the ganglion cell layer, the changes were essentially degenerative, but appearances of cell proliferation by karyokinesis were also present. Baquis observed them also, but attributed them to a simple reaction to irritation, since they were absent after seven days. Tepljaschin confirms this view, though he found many as late as the 15th day (most from 4th to 5th day). They were mostly in the monaster stage, and showed concomitant signs of degeneration, *e.g.*, fatty degeneration, vacuolation (hydropic degeneration), &c.

The changes in the inner reticular layer were principally due to œdema, such as swelling of the fibres and invasion by wandering cells.

The changes in the inner nuclear layer resembled those in the ganglion cell layer, but there were more mitotic

* See my paper on Toxic Amblyopias, Ophth. Review, July, 1901; or Barker's Nervous System, p. 541.

figures, belonging probably, according to Tepljaschin, to Müller's fibres, though some undoubtedly belonged to the nerve cells. Monasters occurred most frequently, and were also accompanied by degenerative changes. Especially noteworthy was the hyaline degeneration of some cells, similar to that described by Oeller⁽¹⁶⁾ in Amblyopia saturnina, Hess⁽¹⁷⁾ in naphthalin poisoning in rabbits, &c. It occurs chiefly in the outer row of cells, *i.e.*, where nutrition from the retinal vessels (in the rabbit) stops.

The outer reticular or inter-nuclear layer is somewhat atrophied, owing to the disappearance of the processes of the degenerating nuclear layer cells: oedema is associated with the atrophy.

In the outer nuclear layer, the nuclei are separated by oedema, the normally visible Müller's fibres being now visible, with their oval, faintly staining nuclei, often showing karyokinetic figures. The latter occur earlier here than elsewhere (2nd day, being absent after the 2nd week). Nuclear division of the nerve cells is only seen a short distance from the wound (4th to 6th day). After the 6th day some of these, situated in parts where destruction is limited to the rods and cones, resemble embryonic forms of these structures. The nucleus sends out a fine process, ending in a knob, through the external limiting membrane, the process being covered by a thin layer of cytoplasm. These resemble the inner limbs of cones, with ellipsoidal bodies (Kostenitsch). The nuclear chromatin of many cells in this layer shows degenerative changes, being broken up; so that later the layer becomes thin by destruction of the cells, debris of which is carried into other layers of the retina.

The rods and cones are either destroyed or in extremely degenerated condition, their place being taken by a homogeneous exudate. In places, however, elongated rods and cones were observed, such as have been described by Nettleship⁽¹⁸⁾ in secondary glaucoma, Leber in glioma, Alt⁽¹⁹⁾ albuminuric retinitis, Nordenson in detached retina, &c.

The pigment epithelium is separated from the rest of the

retina by exudate. The cells show fatty degeneration and vacuoles, though some show mitotic figures.

As regards wounds of the *choroid*, a few remarks are found in the same paper by Tepljaschin. The changes are essentially inflammatory and reparative. The tissues are separated by serous exudate and infiltrated by wandering cells, whilst karyokinetic figures form a distinct feature in vertical sections. They were principally "internal to the chorio-capillaris," in the layer described as the *musculus chorioideæ* in rabbits by Hällsten and Tigerstedt. Karyokinetic figures were also seen in the cells of the muscular layer of the walls of the large choroidal vessels.

The most important researches upon the healing of wounds of the *sclerotic* are those of Krückmann,⁽²⁰⁾ Franke,⁽¹⁾ and Støwer.⁽²²⁾ The two latter operated upon rabbits, the former examining wounds of a duration of 4, 8, 12, 24 hours, and every other day up to 18 days. Krückmann paid most attention to the changes during the first 24 hours, but also continued the investigation up to 120 days: he experimented upon guinea-pigs, rats, cats, and dogs as well as rabbits.

According to Krückmann, the invasion of the wound and neighbouring parts by leucocytes is the prominent feature 4 to 6 hours after the operation. These leucocytes are poured fourth from all the blood vessels available, viz, those of the episclera, choroid, and such sclerotic vessels as are to be found. They are carried from all sides into the wound, which they block, the groups being thickest along the edges. They penetrate into the dilated lymphatic channels between the scleral lamellæ ("Infiltrations-Scleritis" of Alt). The meshes of the *suprachoroidea* are also packed with them. Their function is largely a phagocytic one, directed to the removal of the parts injured beyond repair. The edges of the wound become smooth and glazed, so that the process differs in no essential from that which occurs in other parts of the body. In the course of the 2nd day the leucocytes

begin to disappear, their duty as scavengers having been accomplished.

Franke describes the new formation of round and spindle-shaped cells during this period, by a process of amitotic division. (The need for rapid increase of cells in all acute inflammatory processes results in division by fission, gemination, &c., ordinary karyokinesis being apparently too slow. This is seen *par excellence* in the cornea.) It is not surprising that some increase of the cells present should occur at this early stage, but it is probable that most of them are leucocytes (Krückmann, Stoewer), and that the process described by Franke plays a very subsidiary part.

Franke observed the evidences of karyokinesis after 43 hours, which agrees well with the time assigned by Krückmann for the commencement of the second stage, viz., the process of repair. By this time the detritus and perhaps much of the fibrinous coagulum which formed a large part of the inflammatory exudate have been removed by the agency of the leucocytes, and these themselves have in turn largely disappeared. It is now that the activity of the fixed tissue elements forms a leading feature, and, as in other parts of the body, the blood vessels are the most important. In the episcleral tissue and conjunctiva, in the interstices of the neighbouring muscle fibres, and in the choroid, many cells are seen dividing by mitosis, but especially those belonging to the adventitia of the blood vessels. These (probably including the plasma cells) proliferate rapidly, forming spindle-shaped cells, *i.e.*, embryonic fibrous tissue, which invade the wound area, accompanied by new formed capillaries. Many types of cells are seen in many stages of proliferation, but besides those already mentioned endothelial cells are very prominent. The scanty scleral corpuscles are not inactive, but also proliferate. They do not appear, however, to invade the wound area until a later period. The vitreous has a purely passive part in the process, except that it becomes fibrillated (Franke). The retina is also passive, becoming glued down to the choroid

and locally degenerated. (The retinal vessels probably play a small part in common with those of the choroid.)

Düffing⁽²³⁾ examined an eye microscopically four weeks after a double perforating wound of the sclerotic by a small saw. He found that the fibres of the scar now had the same direction as those of the normal sclera, and passed imperceptibly into the surrounding normal tissue. This result was confirmed by Franke's experiments on rabbits. (It is at this stage in all probability that the normal sclerotic corpuscles manifest their influence. They probably reproduce themselves slowly and partially replace the scar tissue. It is not unlikely, too, that they influence the polarity and character of the newly formed fibrous tissue, tending to gradually mould the new cells to their own type. Such an "infective" influence of one cell upon its neighbours is not uncommon in many pathological conditions (*e.g.* new growths), but where the injured normal cells are of a high degree of differentiation, the process usually stops short at a lower grade, as is seen in the latest stages of scars in the cornea. These become more allied to sclerotic cells than to corneal corpuscles, possibly a form of atavism. In the case of the sclerotic itself, the lowly grade of cell is more readily approximated by the new formed corpuscles.)

EXPERIMENTS ON MONKEYS.

Method.—In my experiments, operations were performed upon six monkeys. The pupils having been previously well dilated by the instillation of atropine, the animal was anæsthetised with ether. The fundus was examined ophthalmoscopically to see that it was normal, and the conjunctival sac was washed out with weak solution of perchloride of mercury. A speculum was inserted, and the eye fixed by fixation-forceps, held by an assistant. A Graefe's cataract knife was then introduced into the eye 3 or 4 mm. behind the corneo-scleral margin, at either the nasal or temporal side, thus avoiding dangerous injury to the ciliary body

and minimising injury to the retina. The knife was passed across the eye through the vitreous to the opposite side, and the retina wounded there to the required extent, the position of the point of the knife being in some cases observed by the ophthalmoscope (direct method). The ophthalmoscope was especially used in lesions near the disc or macula. In other cases, the wound was made without ophthalmoscopic examination, the slight resistance encountered being sufficient to show that the retina had been reached. The exact position and nature of the wound were subsequently determined by ophthalmoscopic examination, which was repeated after an interval of a few days, and also shortly before killing the animal. The lesions were all investigated macroscopically by a suitable section of the eye post-mortem, and were then prepared for microscopic examination.

There was usually no loss of vitreous during the operation, but a small bead escaped in two cases, without, however, causing any untoward result. The wound of entrance healed with great rapidity in all cases. There was slight hyperæmia of the conjunctiva for a day or two, but this quickly passed off, and the animal looked perfectly normal.

The monkeys were chloroformed to death from a fortnight to three weeks after the injury.

The primary object of the experiments was to trace the degenerations in the optic nerves, chiasma, and tracts. These results are recorded elsewhere.

The eyes were hardened in 10 per cent. formol, frozen, and bisected in the direction most suitable for examination of the particular lesion—generally equatorially. The part to be investigated was passed through alcohols, embedded in celloidin, and cut.

Experiment I. Rhæsus. Right Eye.

16.x.01. A small lesion, about 2 mm. long, in a direction tangential to the disc, was made near the equator in the lower nasal quadrant. There was a little hæmorrhage; the

area of pigmentary degeneration was very little larger than the lesion.

31.x.01. Killed.

Microscopical Examination.—Cornea ; a.c., iris and lens normal. The posterior wound passes through the retina and choroid, and just through the sclerotic. The edges of the sclerotic are turned inwards and separated by a plug of new formed fibrous tissue derived from the episcleral tissue. This forms the centre of a mass of more fully developed connective-tissue which extends far into the vitreous (Fig. 1). Anteriorly it spreads out and branches, long fine filaments spreading out as far as the ciliary body. The ciliary body is not inflamed. The non-pigmented cubical cells of the pars ciliaris retinae are irregularly elongated, and appear in places to have definitely proliferated. The inner ends are in contact with extremely delicate filaments made up of long spindle-shaped and branching-cells, the filaments lying almost parallel to the surface, sweeping round in a wide curve towards the lens, and then back to be lost in the mass of tissue springing from the wound. Scattered leucocytes, few in number, lie upon the pars ciliaris retinae and pervade the new formed tissue. They are quite typical in their appearance, though they belong to different kinds of white cells, but no appearances in any degree suggestive of transition into spindle-shaped cells are seen. Many of the leucocytes look perfectly normal, many others are obviously disintegrating. Many cells contain pigment granules in their cytoplasm (Fig. 2), and in places free pigment granules are abundant (Fig. 3). Most of the pigment-containing cells are undoubtedly leucocytes, and none can be definitely stated to be true pigment cells (Fig. 2.) They and the free granules are especially abundant near red blood corpuscles, of which there are comparatively few in this eye, no large vessel having been wounded in this experiment. Where they occur they are usually arranged in layers between the parallel fibrous filaments: there is no evidence of new capillary formation in the anterior part of the eye.

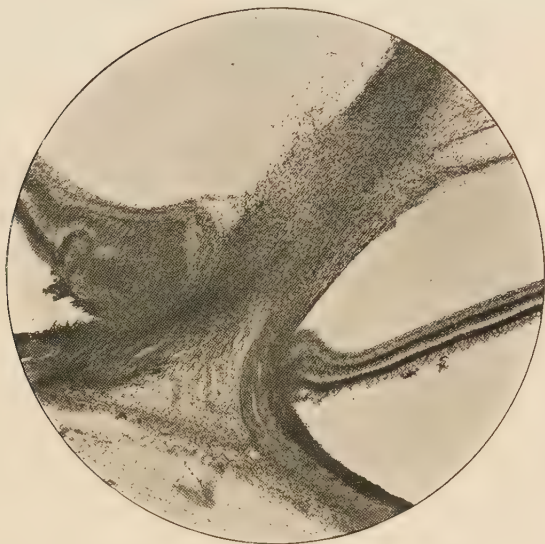


FIG. 1. $\times 25$.

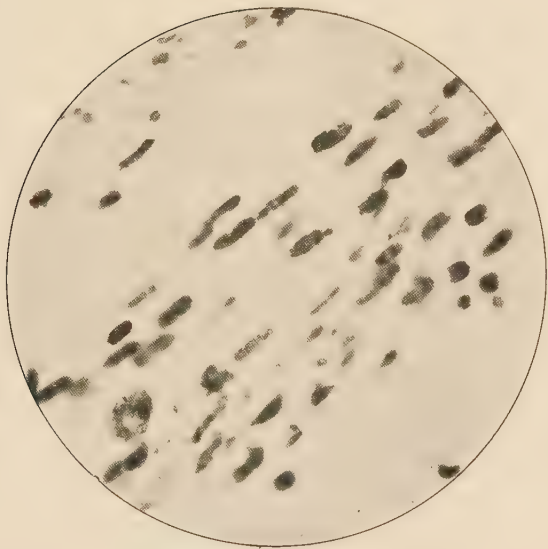


FIG. 2. $\times 300$.

PARSONS—Wounds.

Considering next the main mass of tissue filling the wound, the central core, pyramidal in shape with the apex forward, derived from the episcleral tissue, contains more leucocytes than the remainder. In the centre is a widely-dilated, thin walled new vessel, containing red corpuscles. The leucocytes and some pigment cells are most marked near this vessel. Covering this pyramidal process of episcleral tissue are the in-turned edges of the sclerotic and choroid, outside which the very slightly altered retina is adherent. (The general detachment of the retina in the figure is due to the preparation of the specimen, and was not present when the eye was bisected.) The edges of the sclerotic can be made out in the sections, though they are rounded off and capped with fibrous tissue, which is furthest developed in this situation. The choroid spreads out and is lost in a more highly nucleated connective tissue, amongst which pigment cells are seen: these dwindle rapidly as the tissue is traced inwards. The main mass spreading out into the vitreous consists of closely packed laminae, made up of imbricated spindle-shaped and branched cells, with long oval nuclei. The tissue is most organised at the base, spreading out into processes which extend far into the vitreous and consist of looser tissue of the same kind. Here the shape of the cells is most easily demonstrated (Fig. 4). Interspersed amongst the embryonic connective tissue cells are a comparatively small number of leucocytes, recognised by the deeply stained round nuclei, and a few endothelial cells. The latter are recognised by their large oval (but little elongated) faintly staining nuclei, with deeply stained nucleoli. They are seen with difficulty in the base of the mass, where the tissue is very compact, but deeper in the vitreous they become prominent, and in places are extremely numerous (Fig. 3).

The retina still retains its layers intact, and is only slightly altered even close to the wound. Here there is slight oedema of the inter-nuclear layer. The pigment epithelium, rods and cones, and the nuclear layers are normal.

The nerve-fibre layer and the vessels appear normal, except peripheral to the wound where many of the ganglion cells have degenerated, and the nerve-fibre layer contains many round cells. These are not conspicuous in other parts of the retina.

The choroid is apparently normal except close to the wound. It is deeply pigmented in the monkey, and it is impossible to make out its finer structure without bleaching, which would have spoiled more important structures. Near the wound there is an enormous development of new fibrous tissue growing directly into the proliferating mass, which is evidently largely derived from this coat. There is no evidence that the sclerotic takes any part in this process, but this point is better demonstrated in other specimens.

The optic nerve showed degeneration when examined by the Marchi method. Degenerated fibres were scattered in small numbers over the whole transverse section, but there was a well-marked aggregation on the nasal side corresponding to the retinal wound. (The degenerations in all these monkeys are described in detail elsewhere.)⁽²⁴⁾

Experiment II. Jew. Left Eye.

30.x.01—A rather larger lesion, about 3 mm. long, was made in a direction tangential to the disc a little in front of the equator in the lower temporal quadrant of the retina. There was practically no hæmorrhage, and the pigmentary degeneration was limited to the lesion.

18.xi.01.—Killed.

Microscopical Examination.—Cornea, a.c., iris and lens normal. Part of the wound through which the knife entered the eye is seen in Fig. 5. It will be noticed that it passes through the posterior part of the ciliary body, and anterior to the retina proper. It is filled with new fibrous tissue very similar to that described in Experiment I, but projecting only a short distance into the vitreous. This tissue is principally derived from the subconjunctival or episcleral tissue,



FIG. 5. $\times 10$.

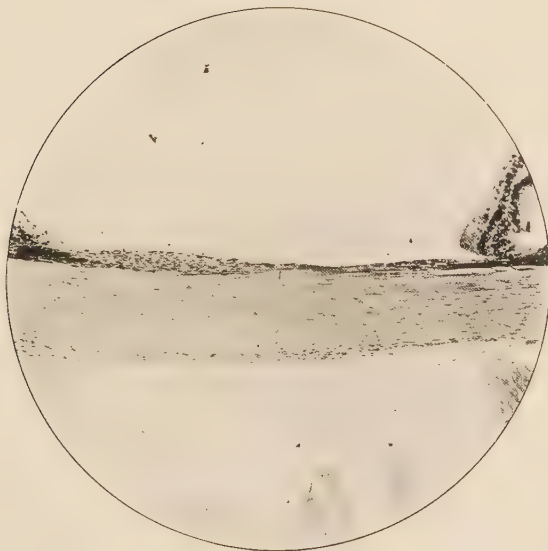


FIG. 6. $\times 60$.

PARSONS—Wounds.



as is proved by other sections, and in much less degree from the uveal tract, as is seen in Fig. 5. The pars ciliaris retinae plainly takes no part in the process at all, except that the pigment cells of this layer sometimes show proliferation, but only in slight degree. The sclerotic, too, is absolutely inert, the edges being clean cut, though slightly rounded off, and the new cells running almost entirely at right angles to them. As mentioned, the ciliary body provides fibroblasts for a modicum of the scar tissue, and some proliferation of its pigment cells also occurs. Pigment is found in small quantities irregularly scattered through the scar, mostly as free granules, some in leucocytes, and some—the smallest part—in pigment cells, most of which are of uveal origin, though some appear to be retinal. It is clear that this lesion produces a minimum of disturbance to the eye, and is probably far less than that produced by the electro-cautery.

The posterior wound, though long (3 mm.), is limited to the retina and choroid, the sclerotic being absolutely intact (Fig. 6). Possibly only the retina was wounded, the choroidal atrophy being secondary: this at least is probable from the minute amount of hæmorrhage, and the limitation of the pigmentary disturbance. It is seen that the retina and choroid are replaced by a well-developed scar of fibrous tissue. The amount of organisation is greater than in Experiment I, on account of the smaller extent and severity of the lesion, and also on account of the longer interval before death (19 as compared with 15 days). The retina and choroid are seen to be closely matted together at the edges of the wound, so that the retina remains adherent here after the processes necessary for microscopical examination. The scar tissue consists of layers of imbricated spindle-shaped cells closely packed together, and having long thin, deeply staining, oval nuclei. They are directly continuous on each side of the choroid, and the retina is merely adherent to them, and seems to have had absolutely nothing to do with their formation. This is very obvious in the stained specimens, where the difference in their avidity for eosin is very

marked, the retina being deep red, and the new cell protoplasm being scarcely stained. The choroidal pigment invades the edges only of the scar, very little in front (Fig. 7), rather farther behind. A few free pigment granules are seen, but beyond these constituents no others can be made out. On the vitreous surface are a few scarcely altered red-blood corpuscles, and a very few leucocytes, one or two of which contain pigment granules.

The retina and choroid were *in situ*, and generally normal. At the posterior edge of the wound the retina is disorganised for a small fraction of a millimetre, and even here there is a normal looking ganglion cell, and the nuclear layers are easily distinguishable, only the rods and cones and the fibre layers having in large part disappeared. Peripherally to the wound, on the other hand, the retina is very much atrophied, the nuclear layers having run together for a considerable distance. Here there are scarcely any ganglion cells, and the reticular layers are degenerated, though the rods and cones are intact over the mid area between the scar and the ora serrata. At the same time, though atrophic, there is no evidence of present or past inflammation. Possibly some of the nuclei may represent leucocytes, but if so, they are not to be distinguished from the nerve cells of the nuclear layers, and there is no new-formed connective tissue.

The choroid was *in situ*, and normal, except at the edges of the wound and over its area.

The optic nerve showed specific degeneration.

Experiment III. Bonnet. Left Eye.

20.xi.01.—A very small lesion was made upon the temporal side near the equator, just below the horizontal meridian. There was no bleeding. Macroscopically there was only a white dot at the site of the lesion.

7.xii.01—Killed.

Microscopical Examination.—Cornea, a.c., iris and lens

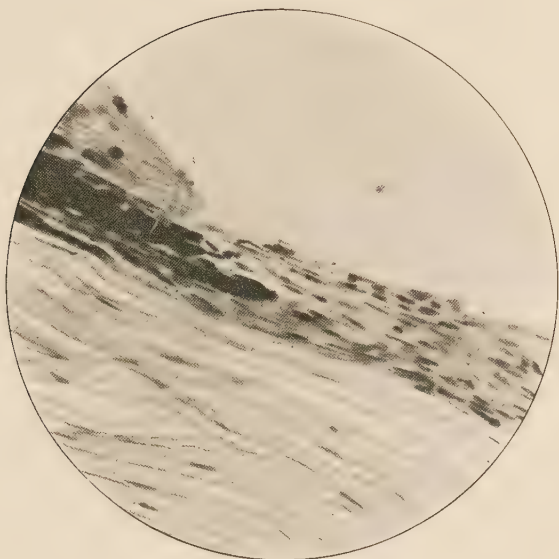


FIG. 7. $\times 300$.

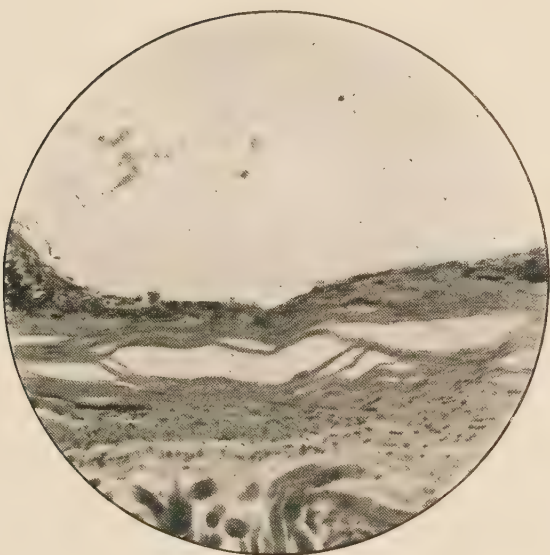


FIG. 8. $\times 120$.

PARSONS—Wounds.



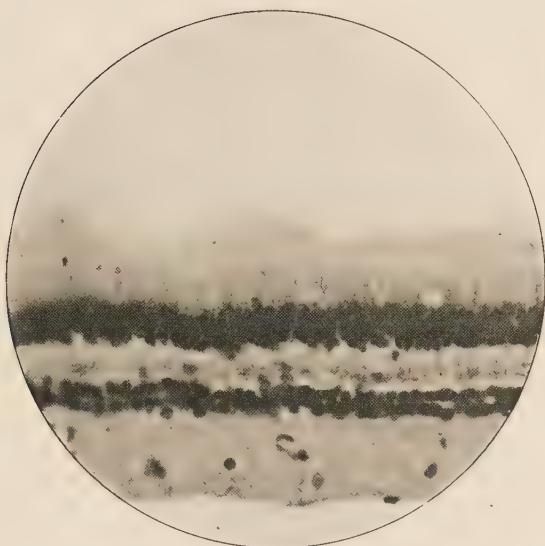


FIG. 9. $\times 300$.

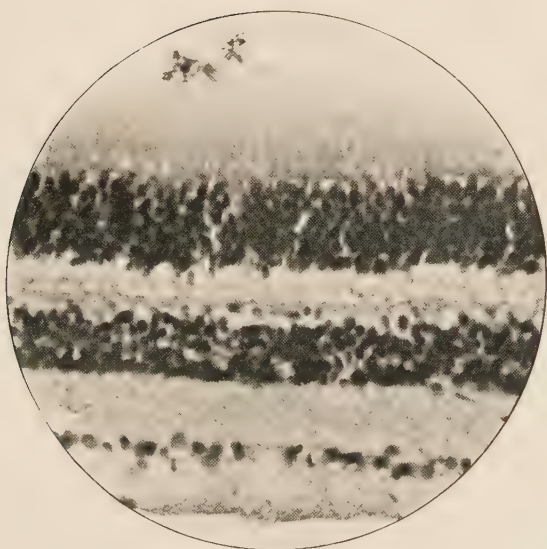


FIG. 10. $\times 300$.

PARSONS—Wounds.

normal. The posterior wound is an extremely small lesion (Fig. 8), involving only the retina and choroid, though probably the inner fibres of the sclerotic were injured: it was certainly not perforated. Microscopically, the lesion resembles that in Experiment II very closely, but rather less scar tissue has been formed. This is of exactly the same type, but is thinner and more pigmented. It is clearly derived from the choroid, though it spreads out at each end and forms two forks, into which the adherent edges of the retina fit.

The retina was *in situ*, and was normal posteriorly up to the adherent edge, which is broader than in II. Here the nuclear layers are clearly defined up to the extreme edge, and some rods and cones can be made out even in the adherent part. Peripherally to the wound the layers are also distinct and apparently normal, with the exception of the extreme sparsity of ganglion cells. Figs. 9 and 10 represent the retina centrally and peripherally of the wound respectively, and the great diminution in the ganglion cells is very obvious.

The choroid was *in situ*, and normal, except that it was atrophied at the wound.

The optic nerve showed specific degeneration.

Experiment IV. Rhæsus. Right Eye.

13.i.02.—The lesion was larger, about 3 mm. long, in this retina. It was on the temporal side, a little behind the equator, and extended above and below the horizontal meridian. There was slight hæmorrhage, and post-mortem there was an oval area of pigmentary degeneration, with axes of about 4 mm. by 3.5 mm. The retina was firmly adherent to the choroid over this area.

1.ii.02.—Killed.

Microscopical Examination.—Cornea, a.c., iris and lens normal. The posterior wound is particularly interesting: the posterior part closely resembles that in Experiment II,

and it may be noted that the period from injury to death is the same (19 days). The anterior part again closely resembles that in Experiment III, whilst between the two we have an area presenting new features. The scar tissue in the posterior part is exactly the same as that shown in Figs. 6 and 7, except that it extends as a thick layer for a short distance over the retina, which is clearly separable from it, though the retina is much atrophied here and represented only by a layer of persistent nuclei of one of the nuclear layers. In the anterior part there are more layers of fibrous tissue than in Fig. 8, and they are rather better organised, facts which are consistent with the slightly longer period (19 days as compared with 17), and the larger, and, therefore, severer wound. Moreover, there is more pigment proliferation; and near the retinal margin some rounder, more faintly staining nuclei, reminiscent of endothelial cells, are seen amongst the long oval deeply-staining nuclei. The central part is noteworthy, in that there is a considerable patch of atrophic retina persisting (Fig. 12). The choroid has almost disappeared here, and the retina lies almost upon the sclerotic. It is represented by nuclei of one or both of the nuclear layers, varying from one or two to six or eight in thickness. Upon these lies an eosin-staining fibrillated layer with no nuclei proper to itself, such nuclei as occur belonging undoubtedly to vagrant cells. Superficial to this, and separating the lower layers from the vitreous, is the continuation of the scar tissue, here only two or three cell-layers thick. Scattered through all these layers are pigment cells, some of which have all the characteristics of retinal pigment epithelium, and the condition of the retina resembles closely the condition found in many pathological human eyes. Some of the cells of the fibrous layer send off processes at right angles to the surface into the vitreous, especially over the degenerated retina. There are a few blood-corpuscles and one or two leucocytes, here and there upon the surface in the vitreous.

The retina was *in situ*. Posteriorly it is practically

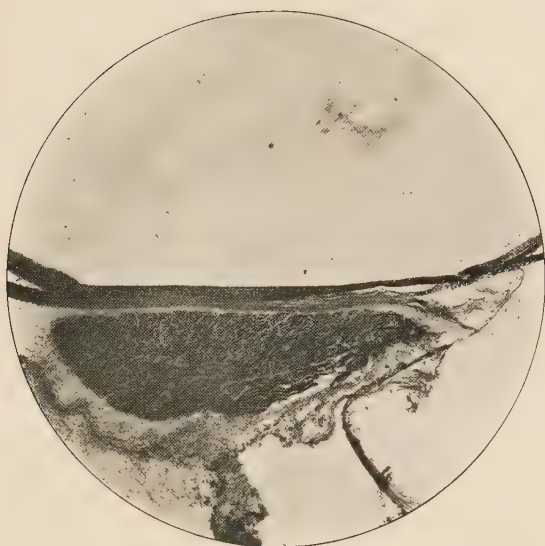


FIG. 11. $\times 17$.

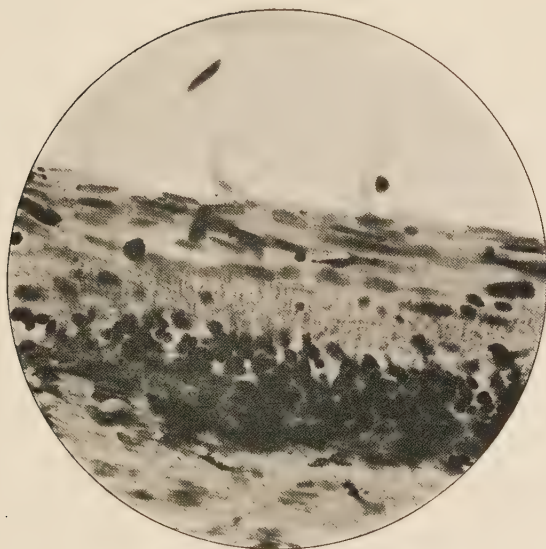


FIG. 12. $\times 300$.

PARSONS—Wounds.



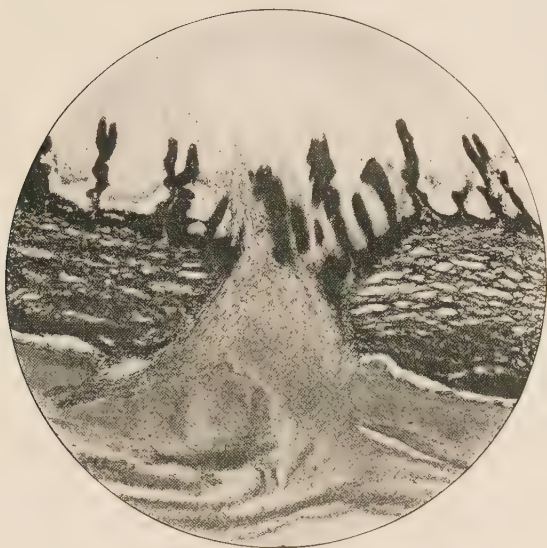


FIG. 13. $\times 25$.

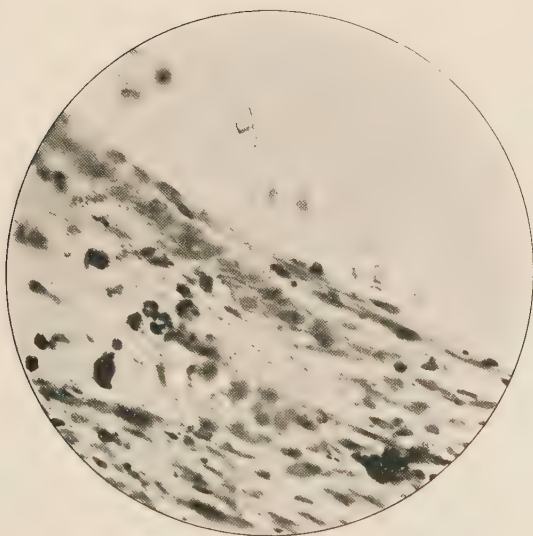


FIG. 14. $\times 300$.

PARSONS—Wounds.

normal, except close to the wound, where the changes are similar to those noted in other cases, except that here, too, we have evidences of proliferation and migration of the retinal pigment epithelium, some such cells being found close to the vitreous surface.

The choroid was *in situ*, and is also normal, except in the immediate vicinity of the wound. It would be difficult to affirm from the appearances in this case alone that the scar tissue was mainly derived from this coat, but in the light of the information obtained from other cases it is possible to see that such must have been the case. At any rate there is no evidence in this case against such a view.

The optic nerve showed specific degeneration.

Experiment V. Rhesus. Left Eye.

14.i.02.—A small lesion was made between the macula and the disc, but at a slightly lower level. It was rather deep, injuring the choroid and sclera, and there was some hæmorrhage.

28.i.02.—The monkey died in the morning; it was dissected about two hours afterwards.

Microscopical Examination.—Cornea, a.c., iris and lens normal. Fig. 13 represents the wound of entry of the knife. The sections were cut eqatorially in this case, but exhibit the same features as in Fig. 5, only on a larger scale. The essential origin of the scar tissue from the episclera is well shown.

The posterior wound shows some characteristics which are less marked in the other cases. Over a small area the sclera has been completely divided; the cut edges, instead of turning inwards, have retracted slightly. The gap is filled with new fibrous tissue, which lies flat upon the normal episcleral tissue, the direction of the cells being, therefore, concentric with the curve of the globe, and not at right angles as in the other perforating wounds. Probably the scleral injury here was wider in extent but less severe, so that no

marked proliferation has taken place into the vitreous. The foundations of the new tissue are the same spindle cells as in other cases, but endothelial proliferation is more marked (Fig. 14). The best defined layer of new endothelial cells is found in this specimen, although it does not show very clearly in the figure. The main origin of the scar from choroid is indicated by the large amount of uveal pigment scattered about, but there are also many proliferated retinal epithelial cells. The episclera appears to be more passive than usual. The retina at the edges of the wound shows the usual type of degeneration, passing rapidly into more normal parts. The degeneration of ganglion cells, &c., peripheral to the wound is well marked. There is some hæmorrhage in the vitreous; but there are very few leucocytes present, and absorption without organisation is going on.

The optic nerve showed specific degeneration.

Experiment VI. Rhæsus. Left Eye.

25.i.02.—A lesion, 2 mm. long, was made in a direction down and out, starting 2 mm. down and out from the fovea centralis. There was considerable hæmorrhage into the vitreous.

15.ii.02.—Killed.

Microscopical Examination.—Cornea, a.c., iris and lens normal. The posterior wound penetrated all three layers. Fig. 15 represents the appearance of sections of the wound. The cut edges of sclera are close together, the small space being filled with new tissue principally derived from the choroid, but partly from the episclera. There are many pigment cells in it. Only the cut edges of the retina appear to have suffered much—where they are bound down to the choroid and sclerotic. A stream of fibrous tissue passes forwards into a mass of red corpuscles lying in the vitreous. A few pigment cells, endothelial cells, and leucocytes are interspersed here and there. Organisation has proceeded farther than in any of the other cases in accordance with the

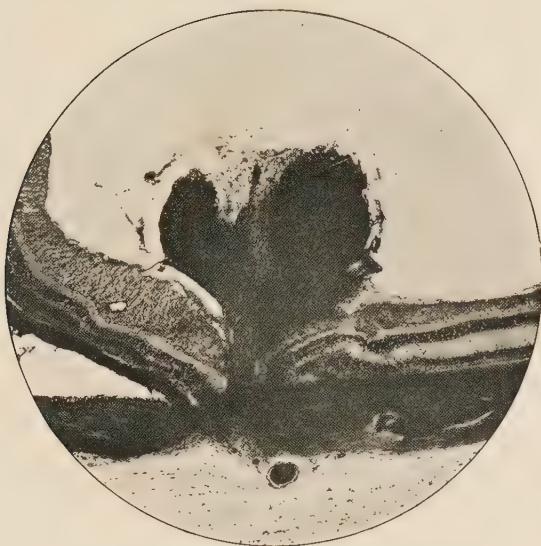


FIG. 15. $\times 28$.

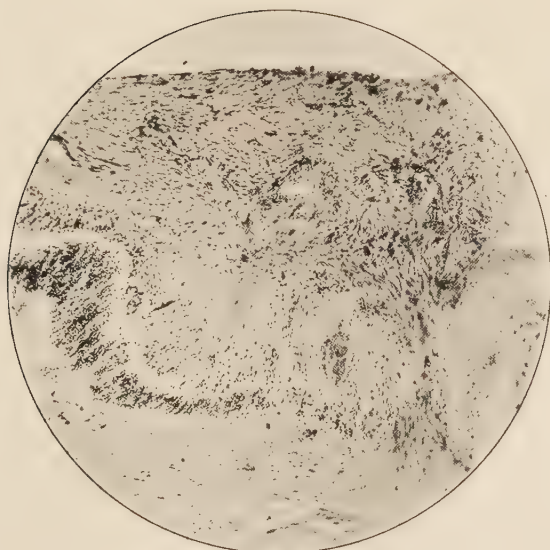


FIG. 16. $\times 60$.

PARSONS—Wounds.

longer interval after the wound. Masses of red corpuscles are found elsewhere in the vitreous, undergoing absorption, but with only small traces of organisation in the form of fibrous filaments in and around them. Other parts of the eye show remarkably little change.

The optic nerve showed specific degeneration.

CASE I.

T. G. (6372), male, æt. 19, was admitted to the R.L.O.H. on 6.v.02, under Mr. Holmes Spicer. On the previous day he was struck by a piece of steel in the R. eye, whilst rivetting.

6.v.02.—*R. eye.* Much conjunctival and ciliary congestion. Small perforating wound of cornea on nasal side near periphery. Hypopyon. Lens probably wounded. Pupil irregular, dilated. White haze in vitreous; no red reflex. V. = p.l. T. —.

L. eye. V. = 6/6.

7.v.02.—Applied to Haab's magnet without result.

9.v.02.—*R. excision.*

PATHOLOGICAL EXAMINATION.—Eye hardened in 10 per cent. formol, frozen, and bisected horizontally through wound.

Macroscopic Examination.—Cornea—wound, with iris adherent. Lens—wounded, and drawn up to corneal wound. Vitreous—contains blood and leucocytes. A sector of steel, about 3 mm. long, was found deeply and firmly embedded in the upper nasal quadrant, a little behind the equator.

Microscopical Examination.—Cornea—slight œdema of epithelium and substantia propria; the wound shows considerable advance towards repair, being partially cicatrised. A.c.—good; angles and anterior surface of iris and lens covered with leucocytes; canal of Schlemm widely dilated and filled with blood. Iris—some iritis, but this is chiefly confined to vicinity of injury, and is less than might be expected. Lens—wounded; capsule torn and convoluted; lamellæ separated at site of injury by wedge-shaped plugs of leucocytes; there is very marked and well-advanced development of new fibrous tissue around the torn capsule in the neighbourhood of the injury. Interspersed amongst the new fibres are pigment cells and red blood corpuscles. Ciliary body—congested. Vitreous—contains red

corpuscles and leucocytes. Retina—looks practically normal except in the immediate neighbourhood of adhesion of f.b., but the vessels are dilated and filled with red corpuscles, and there is some round-celled infiltration of the adventitia. Choroid—normal, except at the same region, where it is enormously congested; even here, there is but little leucocytic infiltration. At the site of injury and lodgement of the f.b., the retina is adherent to the choroid, which is, in turn, knitted to the sclera. The actual bed of the f.b. is a mass of leucocytes and blood corpuscles lying on choroid, which is filled with round cells and pigment cells, the retina being quite destroyed here with the exception of a few vessels. (Fig. 17 is taken from this part.) A little peripherally, however, the change is very different, a well-marked capsule of fibrous tissue having already formed (Fig. 16). Quite a large mass of fibrous tissue has been formed, lying upon a small area of degenerated retina, which suddenly passes on each side into almost normal retina. The fibrous tissue has thin extensions on each side over the quasi-normal retina, gradually thinning off and disappearing. Many proliferated retinal pigment cells are caught in the meshes of the connective tissue. A coarse strand of fibrous tissue is seen passing from the choroid through the degenerated retina into the main mass, whilst the remainder of the tissue is directly continuous with the adventitia of the retinal vessels which have persisted in this part. These features are so marked as to leave little doubt that this new-formed fibrous tissue is directly derived, on the one hand from the choroid, and on the other from the adventitia of the retinal vessels. The choroid underlying this atrophic retinal patch itself consists of cicatricial tissue, passing on each side with but little gradation into the contiguous inflamed choroid.

CASE II.

F. G. H. (6418), male, æt. 50, was admitted to the R.L.O.H. on 7.vii.02, under Mr. Lang. He had been struck in the L. eye on the same afternoon by a fragment of steel.

7.vii.02—*L. eye*. F.b. removed from between the lips of wound by forceps. There was a horizontal wound involving

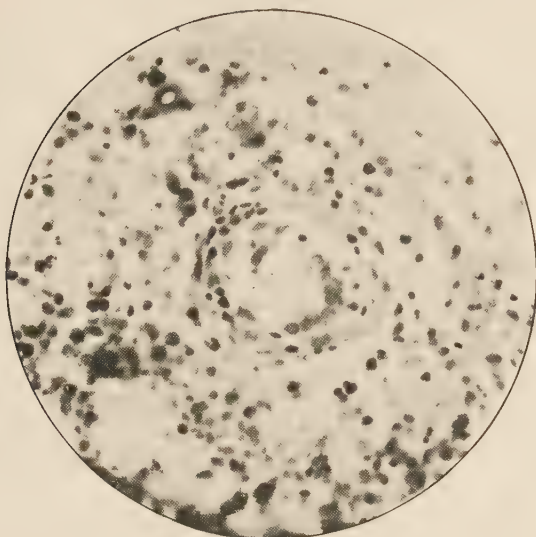


FIG. 17. $\times 300$.

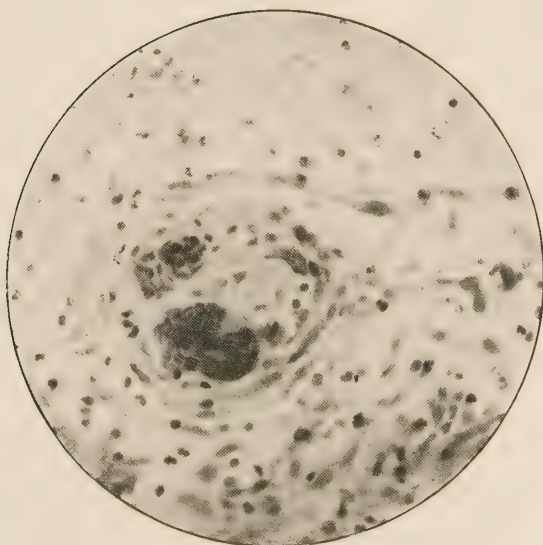


FIG. 18. $\times 300$.

PARSONS—Wounds.



both cornea and sclera, to the outer side, in the horizontal meridian. Aqueous—turbid: hyphæma. Iris—adherent to corneal wound; iritis.

R eye. $V = 6/12 : \bar{c}. +0.75 \text{ sph.} = 6/5.$

Haab's magnet was applied without result. Iridectomy of the adherent iris was performed.

The patient failed to present himself for X-ray examination.

14.vii.02. Hypopyon.

15.vii.02. L. excision.

PATHOLOGICAL EXAMINATION.—Eye hardened in 10 per cent. formol, frozen, and bisected horizontally through the wound.

Macroscopic Examination.—Corneo-scleral wound to outer side; lips infiltrated. Iris—coloboma outwards; iris elsewhere covered with lymph. Lens—traumatic cataract; lens drawn up to wound. Vitreous—adherent to wound; traversed by white filaments; some blood and pus. Retina, choroid and sclera—perforated near posterior pole, slightly external to macula; white filaments radiate forward from this spot to the anterior wound and the lens; others pass forwards from optic disc. There is a large fold of the retina between the disc and the wound, but it does not quite reach the latter.

Microscopical Examination.—Cornea—epithelium irregular near wound: oedema: infiltration of lips of wound, extending for a short distance around. A. c.—much exudate; angles full of leucocytes; canal of Schlemm dilated, and full of red corpuscles. Iris—acute iritis; hæmorrhages. Ciliary body—cyclitis; hæmorrhages; ciliary processes covered with leucocytes and fibrin. Lens—perforated, traumatic cataract; much swelling, especially at posterior wound of capsule; lamellæ separated by wedge-shaped plugs of leucocytes. Vitreous—full of fibrinous exudate, containing leucocytes and red corpuscles. Optic disc—slightly swollen (swelling doubtless diminished by dehydration during preparation); physiological cup filled with leucocytes, which also infiltrate the nerve anterior to the lamina cribrosa in large numbers. Optic nerve—slightly infiltrated; Retina—much congested and infiltrated; layers preserved intact; much folding between disc and wound. Choroid—congested and infiltrated, but less so than in many similar cases. At

the site of the posterior injury the retina and choroid are perforated, and the sclerotic is deeply wounded. The retinal vessels in the immediate neighbourhood survive best and show the best evidences of an almost abortive attempt at repair. Embryonic connective-tissue cells stream out from their adventitia into the surrounding mass of leucocytes (Fig. 18), fibrin and red corpuscles, but the fibrous element soon dwindles down and the main part of the wound is made up of polymorphonuclear leucocytes, phagocytes containing pigment granules, red blood-corpuscles, scattered pigment cells and fibrin (Fig. 19). There are comparatively few endothelial cells; and the connective tissue corpuscles extend but a short distance into the vitreous. A little farther from the wound the layers of the retina are intact, but are infiltrated with round cells, especially the nerve-fibre layer, which is crammed with polymorphonuclear leucocytes, and the inner nuclear layer in less degree. The choroid in this situation is similarly choked with round cells, but here they are almost entirely mononuclear. As is usual in scleral wounds, we find this tissue here almost inert. The edges are clean cut, and only slightly infiltrated, the space being filled with a plug of new fibrous tissue derived from the choroid, its continuity with this membrane being particularly evident.

CASE III.

J. P. (6349), male, æt. 52, was admitted to the R.L.O.H. on 12.iii.02, under Mr. Gunn. On 3.iii.02, he was breaking a piece of iron with a hammer, when a piece flew up and struck his R. eye.

12.iii.02. *R. eye.* Scleral wound on nasal side, immediately behind limbus, about 3 mm. long, directed horizontally. Pupil eccentric and irregular; does not react: post. synechiæ. V = hand movements at 2 feet.

20.iii.02. *X-ray Report.*—"Two stereoscopic skiagrams show the presence of a piece of metal in the vitreous."

21.iii.02. Admitted an in-patient.

R. eye.—Much congested; scleral wound as above described. A. c. good. Atropine mydriasis; posterior synechiæ. Lens apparently clear. Hæmorrhage in vitreous: dull red reflex V = counts fingers at $\frac{1}{2}$ m.: projection good. Tn.

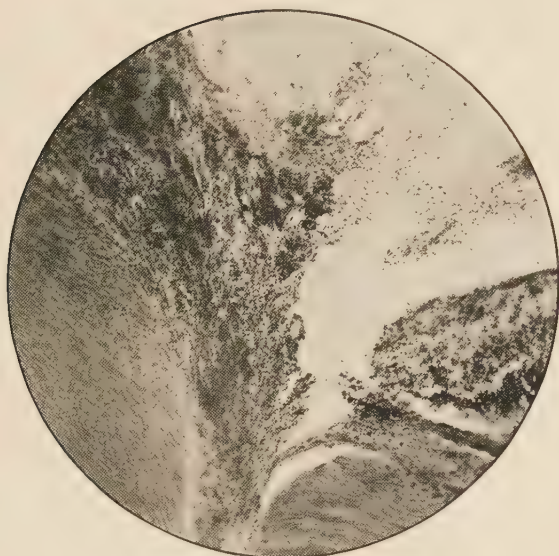


FIG. 19. $\times 60$.

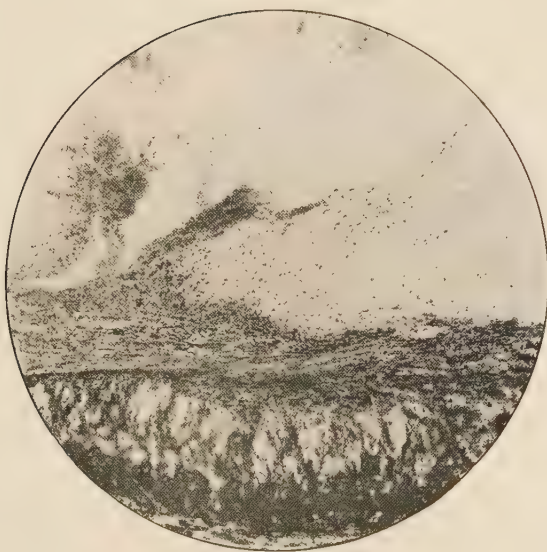


FIG. 20. $\times 60$.

PARSONS—Wounds.

L. eye. Cornea clear. Irritable pupil. V = 6/6 (?), illiterate. Tn.

22.iii.02. R. excision.

PATHOLOGICAL EXAMINATION.—Eye hardened in 10 per cent. formol, frozen and bisected sagittally.

Macroscopic Examination.—A small piece of steel was found firmly embedded in the posterior part of the ciliary body, just anterior to the ora serrata, in a direction downwards and very slightly inwards. There was a small amount of blood in the vitreous, but otherwise the eye looked healthy macroscopically.

Microscopic Examination.—Cornea—normal in greater part of area; slight infiltration and vascularisation of extreme periphery. Conjunctiva—much infiltrated and congested. A. c.—good; upper angle open, lower angle contains a few leucocytes in a fibrinous network; canal of Schlemm dilated, and full of blood. Iris—slight iritis, shown by a few leucocytes throughout stroma, and slight extravasation of blood at the extreme periphery into the stroma. Lens—normal. Ciliary body—acute cyclitis, most marked near site of f.b.: here the ciliary body is much congested, slightly infiltrated with round cells and covered by them. At the site of the wound there is a dense mass of leucocytes lying upon the altered pars ciliaris retinæ (Fig. 20). The leucocytes lie in a meshwork of fibrin, amongst which are a few strands of new-formed fibrous tissue. The striking feature is the intense leucocytic activity and the very slight effort at repair in the form of fibrous tissue development. In the posterior part of the main focus the choroid is much congested; and the retina is intensely infiltrated, pervaded by proliferated retinal epithelial cells, and shows marked connective-tissue hyperplasia. Retina—shows much inflammation and some degenerative changes throughout, these diminishing with distance from the main focus. Choroid—enormously congested everywhere, no gradation being noticeable. Vitreous—filled with scattered leucocytes.

REMARKS.

In considering these lesions there are certain fundamental points which must be continually borne in mind as being of cardinal importance in the process of repair. The first of

these is the fact that the experimental lesions were all absolutely aseptic: there was scarcely any reaction, and after a day or two the eyes looked quite normal; further, there was no trace of pus in the a.c. or vitreous. The pathological cases, on the other hand, were probably all septic, though in varying degree or nature. (They were not examined bacteriologically.) In two (Cases I and II) there is a clinical note that hypopyon was present at some stage, and in these cases there was also a small amount of pus in the vitreous; but in all three there were evidences of contamination, though the virulence of the infection must have been slight in all, as we are only too familiar with the extremely virulent cases in which acute purulent panophthalmitis rapidly supervenes, and all tendencies towards repair are rendered abortive.

The second fundamental point to be held in view is the period which has elapsed between the infliction of the wound and the examination. Thus, in the experiments we have:—V, 14 days; I, 15; III, 17; II and IV, 19; VI, 21; and in the cases:—I, 4 days; II, 8; III, 19.

The third point is the relative severity of the wounds in the various instances; and here many factors have to be taken into account. Of prime importance is the implication of the choroid, or sclerotic, or both, in addition to the retina; for in no case are we here dealing specially with ordinary perforating wounds (except in the wounds of entry in the experiments), for even where all the coats of the eye were pierced, it was from within and not from without—a point of considerable importance. Further, I think that the injury of any considerable blood-vessel adds enormously to the severity of the wound. Speaking generally, however, they may be classified as follows. All the injuries implicated both the retinal and uveal coats, with the possible exception of Case III, in which the affection of the posterior part of the ciliary body may have been secondary. Experiment III was the slightest wound, and Experiment II was only a little more severe; then comes Experiment IV, in which an appreciable amount of hæmorrhage occurred; then Experiments V,

and I and VI, in all of which the sclerotic was also injured, being perforated in the two latter, of which VI is made the most severe of all by the puncture of a fair-sized vessel. The cases are more difficult to classify according to this criterion, forgetting for the moment the far more essential element of sepsis. Here, I think, the site of the wound of entry plays a prominent part, those in which it is situated in the cornea, involving wound of the lens, leading to much more general disorganisation than when the perforation is purely scleral. From this point of view, then, we may regard Case III as of minimal severity; Case I, with a small, purely corneal wound, as of medium severity; and Case II, with a larger corneo-scleral wound, as of maximum severity. In the cases under consideration, the size, nature, and shape of the foreign body, its probable velocity, &c., were fairly uniform, and we may regard this factor as constant.

Turning now to the histological features in the healing of retinal, choroidal, and scleral wounds, we find that the process is, in its essentials, the same as in other parts of the body, but that in details it is modified by the specific characters of the tissues involved. As elsewhere there is invariably hæmorrhage followed by leucocytic infiltration (Stage I). This is succeeded by organisation or cicatrisation (Stage II). These stages must now be considered in the light of the data obtained, paying due regard to previous work upon the subject—both special (ophthalmic) and general.

(1) *Hæmorrhage*.—It is obvious that even the slightest wound of the mammalian retina must be accompanied by hæmorrhage, since the non-vascular part of the retina lies between two vascular layers. In the peripheral parts the hæmorrhage may be minimal and little more than capillary. Here, mere endothelial walls are ruptured, and they probably play little part in subsequent events. In all cases, however, red corpuscles and leucocytes are set free, together with the plasma which provides some, at any rate, of the precursors of fibrin. In every instance, therefore, the wound is rapidly

filled with a clot, consisting of fibrin, with red corpuscles and leucocytes in its interstices. Now, the hyaloid membrane of the vitreous and the so-called internal limiting membrane of the retina have also been wounded for a corresponding extent, and the blood is thus given access to the vitreous. If a larger vessel has been wounded blood is poured out in the direction of least resistance, *i.e.*, along the track of the knife or f.b. The intra-ocular tension has been lowered, and in some cases nullified, but the consistence of the vitreous offers resistance to an equal distribution of the exudates. The retinal, and probably the choroidal, arteries exist normally in ideal anatomical surroundings for rapid retraction, whereby their elastic coats are able to bring their whole force to bear upon the blood-stream, and thus the outflow is minimised. Where this condition is absent, as in arterio-sclerosis, &c., hæmorrhage is followed by much more serious consequences (unless, indeed, it occurs in the otherwise intact eye, where the normal raised intra-ocular tension affords a similar support).

There is no evidence that the red corpuscles and fibrin play any active part whatever in the subsequent events. We, therefore, proceed at once to consider the leucocytes.

(2) *Leucocytosis*—(a) *The Origin of the Leucocytes*.—We have seen that Tepljaschin agrees with a minority of other pathologists in regarding some of the leucocytes as derived from the wandering cells of the vitreous. For my own part I have failed to find the vitreous play any but a purely passive part in any pathological condition, so that I have come to regard it as inert, and to look upon such terms as “shrinking of the vitreous,” &c., as implying an activity which does not exist. At the same time, only the most painstaking investigation could really prove this to be the case, and the undoubtedly great *relative* inertness of the vitreous elements is sufficient excuse for leaving this point in abeyance.

There can be no doubt that the enormous majority, if not all, of the leucocytes are derived from the vascular (both

blood and lymph) channels. In some animals, the perivascular lymph-sheaths of the retinal vessels are conspicuous, and it is probable that their contained lymph affords its quantum of leucocytes.

As to the question whether all the leucocytes are the result of emigration, or whether those which have already emigrated, divide and multiply, it is probable that the latter view is correct, but my observations give no evidence. It may be remarked that the eye is admirably adapted for the solution of this and kindred questions, all that is required being the examination of earlier specimens by specific methods directed to the particular point.

(b) *The Function of the Leucocytes*.—It can scarcely be doubted that this is exactly the same as elsewhere in the body in similar circumstances. (a) *Digestive*.—By their ferment action they soften and liquefy the necrosed tissues, *i.e.*, those which have been killed by the severity of the injury. The products of digestion, now in solution, are readily carried off by the lymph stream. (β) *Mechanical*.—By their aggregation and fibrin-forming process they form plugs which help to seal up the broken and contused blood- and lymph-channels. This function has also a deleterious action in impeding the flow of nourishment to the part, thus increasing the necrosis, which they further deal with by their digestive function. It also impedes the outflow of effete material, thus leading to unfavourable conditions of vitality, which also must be taken into account. (γ) *Phagocytic*.—It is unnecessary to dilate upon the bactericidal function of leucocytes here, but their phagocytic activity is most easily seen in the very marked way in which they deal with the red blood corpuscles and with the blood pigment of broken down corpuscles (Fig. 2). This function is doubtless applied to all the more insoluble products of disintegration.

Whether the digestive activity of leucocytes is exerted upon the fibrin which they have helped to form, is doubtful. One is familiar with old-standing fibrinous clots containing multitudes of leucocytes, where there is no reason to suppose

that such a process has occurred, and it is probable that the fibrin is too admirably adapted for fodder for the young connective-tissue cells for it to be wasted in this manner.

(c) *The Fate of the Leucocytes.*—My experiments only afford evidence of one destination of the leucocytes, viz., disintegration. This is frequently observed in the broken-down white cells, with fragmented nuclei, and in the occurrence of free nuclei.

It can hardly be supposed that this is the fate of all of them, but I have seen no reason to suppose that they contribute directly to the formation of fibrous tissue. We have seen that the relative proportions of leucocytes to embryonic connective-tissue cells varies enormously at different periods and under different circumstances, especially sepsis, injury of the larger retinal vessels, wound of the choroid, &c. However few or however numerous they may be, they are always absolutely characteristic, and one never finds forms intermediate between them and connective-tissue cells. This I know is diametrically opposed to Tepljaschin's views, but it accords with the observations of Sherrington and Ballance, and of most other pathologists. It is another point which demands reinvestigation by special methods on early specimens.

Mention has been made of the extreme variability in the number of leucocytes found in different stages after injury in different conditions. This is a very striking point, and the most important factor seems to be the bacterial one. None of the cases described were severe cases of septic wound, but one is familiar with the rapid onset of purulent panophthalmitis in many such. Here, the efforts towards repair, which we cannot doubt are exerted, are entirely abortive, and Stage II is never reached. The variability in number, however, is very noticeable in the aseptic cases, and seems to be largely dependent upon the severity of the wound, *i.e.*, upon the injury of large retinal blood-vessels, or of the choroid, or upon actual perforation. Probably the implication of the choroid is the most important factor, and this gives some

support to the hæmic origin of the cells. The more purely retinal wounds with a minimum of bleeding have very few leucocytes, but wherever there is much hæmorrhage the white cells are abundant.

We have now considered the first stage in so far as it affects the actual site of the wound. The changes in the surrounding tissues are very little marked in aseptic wounds, being limited to the ordinary signs of acute inflammation in the immediate vicinity. In septic wounds the inflammatory process is much more widely spread, resulting in congestion (most marked in the choroid), and infiltration with round cells. These changes, however, are amongst the earlier ones of which the experiments and cases offer no good example.

In the second stage, the essential part of the process of healing commences and soon gains the upper hand, consisting of the formation of fibrous tissue, leading to the production of an organised cicatrix.

(3.) *Cicatrization*.—(a) *The Formation of Fibrous Tissue*.—As stated above, we have seen reason to deny the formation of fibrous tissue from leucocytes. We must, therefore, look to the fixed tissue elements for the mother-cells. We are at once confronted with the number of tissues to choose from. Putting the vitreous out of the question, as before, we have in all the specimens the various structures of the retina and choroid to deal with. The true neural elements of the retina for the most part degenerate, the ganglion cells and their nerve-fibres never regenerate, and even if the rods and cones make abortive attempts (Tepljaschin, &c.), these are merely curiosities, and form no essential part of the cicatrix. We are thus reduced to the neuroglial elements of the retina, its blood-vessels, and the choroid.

Proliferation of Müller's fibres has been described in innumerable pathological cases in human eyes; exactly how much credence is to be attached to these cases is doubtful. The normal condition of Müller's fibres is very difficult to determine, except in isolated teased specimens. They are so overwhelmed by the nerve cells in the normal state that

only parts of them can be seen peeping out here and there. In the pathological cases, the nerve elements are invariably more or less degenerated—and then Müller's fibres are said to be hypertrophied and to have proliferated. Confining ourselves only to the specimens reported in this paper, I have failed to find any evidence whatever of proliferation of Müller's fibres. The question cannot be said to be finally settled until it is investigated with this special aim in view, using specific neuroglial stains and examining carefully at various stages. It may, indeed, be found necessary to apply such tests to wounds in very young animals. In ordinary aseptic wounds I have not observed such direct continuity between Müller's fibres and the new fibrous tissue such as is depicted in Tepljaschin's paper, Plate xxii, Fig. 4; whereas his Fig. 28, Plate xxiii, well represents the appearances found in Experiment II, Figs. 6 and 7, and resembles those found in Experiments III and IV, Figs. 8 and 12. Indeed, the differentiation between the two tissues is usually very distinct even by the ordinary methods of staining, but an apparent continuity is not infrequent in pathological specimens. Differential staining can alone determine how far the appearances are deceptive. It is perhaps *à priori* improbable that epiblastic elements should take any very prominent part in a process so essentially characteristic of mesoblastic tissues. Chemical tests may also be valuable in elucidating this point, and it would be interesting to know the relative part played by epi- and meso-blastic structures respectively in other cases of sclerosis of the central nervous system, for, as far as I know, the question has received scant attention by neurologists. It would probably be easier to decide in these cases, and the analogy is so exact that the result would almost certainly be applicable to the retina.

We are reduced, therefore, to the mesoblastic tissues found in and around the retinal blood-vessels and in the choroid. There is ample evidence to show that both of these structures take part in the process, though the latter is by far the more important, chiefly by virtue of mere mass.

The slighter the injury to the choroid, the less is the hyperplasia of connective-tissue, and, though no example can be adduced from the specimens examined, I have little doubt that a pure retinal lesion becomes cicatrised wholly from elements derived from its own mesoblastic elements, *i.e.*, from the connective tissues in and around its vessels. Where the fibrous tissue is seen growing over the normal or degenerated retina (*e.g.*, in Experiment IV in the posterior part (see description) and in Fig. 12), the choroid being intact or not in direct continuity, it is doubtless derived from the retinal vessels alone.

The persistence of the retinal blood-vessels is a striking feature even in the septic cases. When all other parts of the retina have melted away, and are replaced by masses of leucocytes (*e.g.*, Fig. 17), these stand out clearly—widely dilated, often crammed with red corpuscles, or partially or completely thrombosed. The appearances seen under high magnification in these and cognate cases, lead one irresistibly to the conclusion that the cells of the adventitia proliferate, and add to the mass of embryonic tissue. This is seen in an early and feeble phase in Fig. 17, and in a later and strenuous phase in Fig. 18.

Where the wound results in injury to the sclerotic, no new factor is introduced, at any rate in the early stages, unless this coat is perforated, and then the episclera assists in the process in exactly the same manner as the choroid, only in less degree, due doubtless to its inferior vascularity. In anterior perforating wounds, the episclera takes a larger share on account of its relatively greater vascularity here, due to its more intimate association with the extrinsic muscles. Only the fibrous tissue elements in the muscles proliferate, the muscle fibres remaining inert.

The origin of connective tissue (and other cells) from the cubical cells of the pars ciliaris retinae has been much insisted upon from time to time. Appearances indicating this are not wanting in my specimens, but I think they are fallacious. The cubical cells are much altered in appearance

in those cases in which new filaments of fibrous tissue stretch forward through the vitreous as far as the ciliary body. Some of them are stunted, whilst others, often forming groups, are much elongated, so that they become cylindrical. The inner ends of these elongated cells are always attached to the fibrous filaments, and their elongation is probably due to traction. By the time the filaments have reached so far forwards, the posterior mass of new tissue is commencing to shrink—a characteristic common to all cicatrices—and thereby considerable traction is exerted upon the anterior attached ends. The sweeping curves of the filaments are probably conditioned by the effect of the track of the wound in the vitreous upon its normal structure, and results in the ciliary retinal cells being more often drawn forwards and inwards than directly inwards or inwards and backwards.

Having stated so much, it still remains to be shown which of the mesoblastic tissue elements provides the actual mother-cells of the new formation. The specimens provide little evidence for proving this point, one of the most difficult in pathology. Attention may be directed especially to the work of Sherrington and Ballance upon the subject (*vide supra*, p. 219).

(b) *The Behaviour of the Endothelial Cells.*—Endothelial cells are found normally only in the blood and lymph vessels of the retina and choroid, with the possible addition of an incomplete layer lining the hyaloid membrane, and a layer in the choroid which is probably a vestige of the tapetum. It is certain that they proliferate during the repair of wounds and in other pathological conditions. They are most commonly met with in various inflammatory conditions, as a uni- or multi-cellular layer covering the inner surface of the retina. In such cases they may well be derived from the cells lining the hyaloid, but this is purely hypothetical. They seem to vary greatly in numbers and distribution in different wounds, and it is difficult to assign the reasons for this peculiarity. In Experiment I they were present in large numbers in the vitreous, especially in a band,

of which Fig. 3 represents a part; but they are also generally present amongst the embryonic connective tissue, particularly in the early stages. They are not infrequently present also in later stages, and in very chronic inflammatory conditions. I have not seen such evenly arranged layers over the retina in the case of wounds as in other pathological states, but they are recognisable amongst the fibrous tissue in Figs. 12 and 14.

It has been stated that the endothelial cells become changed into new fibrous tissue, and that this is their main function in these cases. I have not seen any evidences of transition states, the two types of cells being usually quite characteristic. I believe it is not yet definitely settled which layer of the embryo they originate in, so that their development does not assist us in determining their probable destination. It is probable that their function in pathological conditions has not, in the past, received the attention it merits.

REMARKS ON RETINITIS PROLIFERANS.

It is unnecessary to enter into details as to the causation and general pathology of Retinitis Proliferans in this place. An excellent *résumé*, with the best recorded pathological examination of a case, will be found in a paper by Mr. Percy Flemming in the Transactions of the Ophthalmological Society of the United Kingdom.⁽²⁵⁾ The crucial point in the pathology of these cases is the explanation of the widespread proliferation and organisation which takes place, and which does not occur in other cases of retinal hæmorrhage. Mr. Flemming attributes this to the "inflammatory process present at the time in the retina and papilla," due to some toxic agent (*e.g.*, that of diabetes, syphilis, or nephritis). I think the sequence is probably as follows. Some toxic condition leads to a retinal hæmorrhage. If it is situated in the peripheral parts of the retina, or is due to rupture of the smaller vessels nearer the papilla—in other words, if it is a

small hæmorrhage—no large proliferation of new tissue will result. A scar will result from the organisation of the clot through the medium of the scanty mesoblastic tissue of the walls of the smaller retinal vessels. If, however, a large hæmorrhage occurs, it will be in the neighbourhood of the disc, or if caused by repeated hæmorrhages in slightly more peripheral parts, will yet invade the neighbourhood of the larger vessels, *i.e.*, again the neighbourhood of the disc. Now it is around the larger vessels, and *par excellence* upon the disc that the main mass of retinal mesoblastic tissue is situated. At the papilla itself, we have not only the walls of the vessels, but also remnants of the hyaloid artery and a ring of anastomoses with posterior ciliary vessels—in fact, the largest mass of mesoblastic tissue found in the walls of the true optic cup. The nearer the hæmorrhage approaches this point, and the more widespread its traumatic and irritating effects in this immediate neighbourhood, the more tissue will be excited to reparative reaction, and the greater will be the proliferation and organisation. Hence the fact that Retinitis Proliferans invariably springs from the disc or its vicinity. In the periphery there are two factors acting against such proliferation: first, the smallness of the hæmorrhage, which, however, may possibly be increased by repetition or multiplicity and confluence; second, and more important, the small amount of tissue which is capable of proliferating and inducing organisation.

Upon this hypothesis, the toxic agent acts only, or at any rate chiefly, by producing retinal hæmorrhage, and only secondarily, or not at all, by producing an inflammatory process in the retina and papilla. Against the latter hypothesis are the facts that the relatively healthy retina may show no marked signs of any such inflammatory process being present, and that the toxic conditions so frequently present, whilst potent causes of hæmorrhage and even of inflammatory conditions, are, with the possible exception of nephritis, not known to be specially effective in leading to fibrous tissue proliferation.

The experiments described in this paper were performed in the Physiological laboratory, University College, London. I desire to express my thanks to Professor Starling for the use of the laboratory. The expenses were defrayed by a Royal Society grant. The histology was worked out in the Pathological Laboratory, R.L.O.H.

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A CASE OF RETINITIS PIGMENTOSA, WITH PATHOLOGICAL REPORT.

By W. T. LISTER, F.R.C.S.

I AM enabled to bring forward this case of Retinitis Pigmentosa owing to the kindness of Mr. Nettleship, who both gave me the specimens and also supplied me with his notes of the case made 24 years ago. We are both greatly indebted to Dr. F. Pritchard Davies for having sent the specimens to Mr. Nettleship, after the case had been under his care as an inmate of the Kent County Asylum for 20 years.

July, 1878. W. S., male, æt. 38, came to St. Thomas's Hospital complaining that he had always been "near sighted," and had never been able to see in the dusk as well as other people.

His right eye had begun to get worse in 1870; he had been told he had cataract in the eye; and an operation for artificial pupil had been performed downwards. His left eye began to fail in 1876.

R.V. J. 19; c. sp. — 8 D 20/100.

L.V. J. 1 with difficulty at 4 inches; c. sp. — 6 D. 20/70.

Media.—Posterior polar and cortical opacity in each lens—denser in R. than L.

Fundi.—Advanced Retinitis Pigmentosa, with much pigment. The pigmentation was situated in a somewhat zonular area, extending in thinly scattered spots as far as the disc, but ceased, to a great extent, towards the periphery. The optic discs were pale; the vessels were small; there was a myopic crescent and some diffuse myopic changes of the adjacent choroid, but no islands of atrophy of the choroid.

W. S. had had good health; there was no history of syphilis.

Family History.—His mother died insane, æt. 72. He had one brother who could not see in the dusk; one half-brother and

one half-sister, both mentally defective. No consanguinity of his ancestors was known.

It was learnt from his wife, in 1880, that W. S. was suffering from delusions, and, later in the year, Dr. F. Pritchard Davies, Superintendent of the Kent County Asylum, wrote to tell Mr. Nettleship that W. S. was under his care with religious melancholia.

In 1900, Dr. Davies again wrote to Mr. Nettleship, and stated that W. S., who for some years had been totally blind, had just died, æt. 60, and he kindly sent both globes for examination.

Pathological Examination.—Both globes had been preserved in spirit, which had made the tissues, and especially the retina, very brittle. Nothing abnormal was noted before freezing and opening the eyes by an antero-posterior section in one eye and an equatorial section in the other.

The anterior chamber was shallow ; the iris normal ; the lens opaque throughout ; the vitreous was fluid. Retina and choroid *in situ*, but so intimately united that separation of the two was impossible.

The retina in its posterior two-thirds was deeply pigmented, the pigmentation taking the form of an irregular network, which gave it a speckled appearance. (Fig. 1, c.)

The anterior third of the retina (Fig. 1, b), forming a zone about 7 mm. in width, was pale and unpigmented, strikingly different, and sharply marked off from the posterior pigmented portion. (Fig. 1, c.)

The macular region appeared as an oval pale grey area ; the pigmentation here also was much less than in the surrounding parts. There was a well-marked myopic crescent on the outer side of each disc.

The retinal vessels were extremely minute, but with a magnifying glass the main trunks could easily be made out as white lines running over the retina, and, in places, a very fine dark line down the centre of the pale path could be distinguished.

The retina and choroid, as mentioned above, were intimately adherent ; together they could be separated from the sclerotic with difficulty, though in many places they were very adherent.

Portions of the combined retina and choroid were mounted "on the flat" (Figs. 1 and 2), to show the distribution of the pigment and its relation to the blood-vessels, and microscopic sections were made of the—

- (1.) Lens.
- (2.) Optic nerve and disc (longitudinal).
- (3.) Retina and choroid.

Sections of the lens show the ordinary cataractous changes; nothing distinctive could be made out at the posterior pole.

Sections of the optic nerve and disc show the nerve to be more fibrous than usual, the septa being thicker than normal and particularly well marked. (The specimen having been preserved in spirit, no special stains were employed to show degeneration of the nerve fibres.)

The optic disc is slightly cupped and is covered by laminated connective tissue, which is continued into the surrounding retina, and takes the place of the nerve-fibre layer.

Sections through the retina show appearances similar, on the whole, to those described by previous observers.

Only in the parts close to the disc and macula is there any trace of the normal retinal layers. In the darkly-pigmented area the retinal tissue is completely atrophied, and its place is taken by a loose connective tissue.

Taking, first, the sections of the parts close to the disc and macula:—

The *nerve-fibre layer* shows no thickening, nor is there any adventitious layer formed in the place of the *membrana limitans interna*, as in the specimens described by Leber and Landolt. The nerve fibres have been replaced by loose laminated connective tissue, as mentioned above, which is continuous with that found on the surface of the disc.

The *ganglion layer* is well seen in the macular region, but the cells are not so closely packed as normally.

The *inner reticular layer* can be distinguished in places near the disc and macula.

There is only one *nuclear layer* visible, and this is much thinner than either of the two layers that are usually found. (As there are not two nuclear layers in any part, it is impossible to say for certain whether this remaining layer represents the outer or the inner nuclear layer or both; but from its special relation to the inner reticular layer and the ganglion layer, it probably represents the inner nuclear layer.)

The *layer of rods and cones* is altogether absent. Its place has been taken by laminated fibrous tissue, between the layers of which are seen numerous oval nuclei (Figs. 3 and 4). This tissue lies next to the pigment epithelium on the outer side and to the nuclear layer on the inner side.

The pigment epithelium is a well marked layer in the macular region.

In the sections through the retina outside the central area practically all traces of the normal structure of the retina are lost. Here and there a short line of pigment cells at the site of the pigment epithelial layer is seen, and again somewhat linear groups of nuclei resembling those in the nuclear layers are found, but as a whole the tissue representing the retina consists of connective tissue, which is loose and reticular towards its inner aspect, and laminated and much more dense towards its outer aspect (Figs. 3 and 4).

In this connective tissue are embedded the blood-vessels. These have thickened and deeply-pigmented walls, and in most the lumen is blocked (Figs. 3 and 4). Some of the vessel walls have retained their laminated structure (V_2), but others have undergone hyaline degeneration, and are structureless (V_1).

There are a few irregular excrescences from the choroid in the outer part of the connective tissue; these also are pigmented, and probably have been derived from the lamina vitrea, but this layer cannot be made out.

On examining the portions of retina and choroid mounted on the flat (Fig. 2), the network of pigment is clearly seen; and when viewed under the microscope it is evidently on a

different level from the choroidal pigment. One sees at once also that the pigmentation follows to a great extent the course of vessels, but these vessels are neither the main retinal trunks, nor are they capillaries, but are probably small arterioles from which the capillaries would be given off. I think it is quite possible that some of these vessels are of new formation.

Here and there more diffuse patches of pigment are seen, and some of these are probably the pigmented excrescences from the lamina vitrea.

The choroid is atrophied, and the chorio-capillaris layer has disappeared. But it is a striking fact that the choroidal vessels seen in the sections have not got thickened walls. This corresponds with the appearance of the choroidal vessels seen on the flat, which have no irregular vermicular course as is so commonly seen in cases of sclerosis of the choroidal vessels.

Beyond the description of this case I have little to contribute to the pathology of the disease. The changes found in cases of retinitis pigmentosa, taken as a whole, are concentric atrophy of the retina with pigmentation and degeneration of the retinal vessels, associated with a variable amount of chronic inflammatory change.

Some hold that these changes are brought about by primary vascular disease either of the retina or choroid. But the concentric defect corresponds with a *nerve distribution* rather than a *vascular* distribution, and therefore I think we must look for a degeneration commencing primarily in the nervous tissues rather than in either vascular system.

There is undoubtedly a group of cases with sclerosis of the choroidal vessels and—probably a secondary—pigmentary degeneration of the retina; but these cases must be classed separately, for they are often unsymmetrical or even entirely monocular, whereas typical cases of retinitis pigmentosa are symmetrical, and no changes are seen in the choroid or its vessels, which, if present, would be especially apparent owing to the atrophy of the retinal pigment.

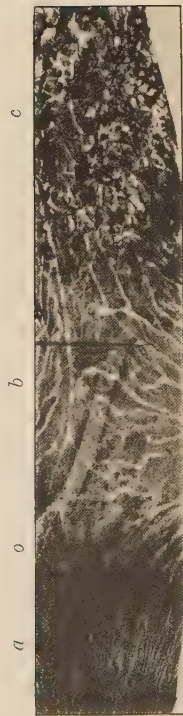


FIG. 1.



FIG. 2.

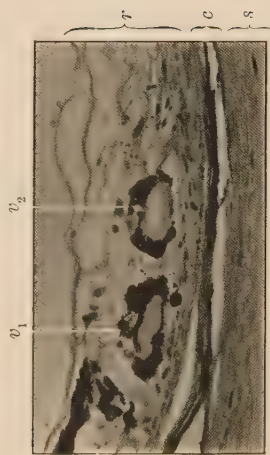


FIG. 3.

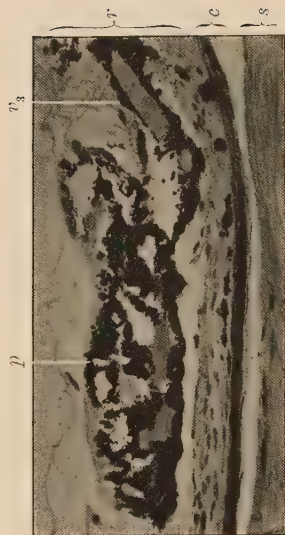


FIG. 4.

LASTER—Retinitis Pigmentosa.

FIG. 1.—Strip of retina and choroid mounted on the flat. (*a*), ciliary body; (*o*), ora serrata; (*b*), unpigmented zone of the retina, showing the choroidal pigment and the course of the choroidal vessels; (*c*), pigmented portion of the retina.

FIG. 2.—Pigmented portion of retina with choroid, mounted on the flat, under higher magnification. The black pigment in the retina is easily distinguished from the paler choroidal pigment. The black retinal pigment is arranged (1) in lines, following the course of blood-vessels, and (2) in patches. The white lines between the areas of choroidal pigment mark the course of the choroidal vessels.

FIG. 3.—Section through retina (*r*), choroid (*c*), and sclerotic (*s*). The retina is atrophied, its place being taken by connective tissue, which is loosely arranged internally and laminated externally; between the layers can be seen numerous oval nuclei.

Embedded in the connective tissue are seen the pigmented vessels in cross-section (v_1, v_2), in both of which the lumen is blocked, but the walls of (v_2) still retain their laminated structure.

FIG. 4.—Also taken through retina, choroid, and sclerotic; shows in the main the same points as Fig. 3.

In addition (v_3) is a pigmented vessel cut longitudinally, and at (*p*) the section passes through one of the larger pigmented patches seen in Fig. 2.

THE OPHTHALMIC ARTERIES IN THE RABBIT AND DOG.

By E. E. HENDERSON, F.R.C.S.

IN any experiments on the intraocular circulation one of the lower mammals must, as a rule, be employed. As the dog and rabbit have been the animals most employed for this purpose, it is of importance to the experimenter to ascertain the anatomy of the orbital arteries in these animals, and so note the differences from the human type. For this purpose six dogs and six rabbits have been injected with plaster of Paris, and careful dissections made on each side. As this injection only penetrates to the smaller arteries the more minute anatomy cannot be studied in this way. I propose, in this note, only to deal with the gross anatomy.

The only text-book devoted to the anatomy of the dog with which I am acquainted is that of Ellenberger and Baum.⁽¹⁾ In dealing with the point now under discussion these authors refer to the work of Bellarminow, but do not give the reference, and I have been unable to consult the original paper. The standard authority for the anatomy of the rabbit is Krause.⁽²⁾

As is well known the blood supply of the eye as we descend the animal scale tends to be derived more and more from the external carotid. It is therefore only to be expected that individual variations would be of frequent occurrence. I will first briefly describe the results of my dissections, and compare them with the account of the blood supply of the eye, as given by the authors referred to above. The rabbit, as being apparently of a somewhat more standard type, will be taken first.

The common carotid in the rabbit gives off the thyroid artery and the ascending pharyngeal. In addition, Krause adds that the laryngeal may come from it. At the level of the hypoglossal nerve the artery divides into the internal

and external carotids. The former is much the smaller, and runs without branching to the bulla tympani, and enters the skull by the carotid foramen. It then winds round the lateral side of the body of the sphenoid bone, and after crossing the oculo-motor nerve, gives off the anterior communicating and superior ophthalmic arteries. It ends by dividing into the anterior and middle cerebral. In four of my dissections I have been able to trace a fine branch of communication between the internal carotid, as it lies on the side of the body of the sphenoid, and the internal maxillary close to the origin of the inferior ophthalmic artery. The external carotid gives from its inner side the laryngeal, lingual, and external maxillary in that order from below upwards. The last-named artery gives off the facial. From the posterior wall is given off the occipital. A little below the neck of the jaw the artery divides into the superficial temporal and the internal maxillary. The former gives off the transverse facial and the auricular. The internal maxillary runs deep to the internal pterygoid behind the lower jaw. It gives off the tympanic, the inferior alveolar, some muscular branches, and the middle meningeal. It then passes through the pterygoid canal, and gives off the inferior ophthalmic. It ends by supplying a superior alveolar branch, and divides into the infraorbital and pterygo-palatine arteries.

So far in my dissections the arrangement of the branches of the carotid arteries are in entire agreement with the description given in Krause (*loc. sup. cit.*, p. 183). I have, therefore, followed his nomenclature. I now quote in full his description of the ophthalmic arteries.

“The inferior ophthalmic artery runs on the anterior surface of the upper part of the great wing of the sphenoid, bends forward over the optic nerve, and reaches its anterior side. It there anastomoses with the superior ophthalmic artery. Its branches are as follows:—1. Lacrymal, which appears through the posterior supraorbital foramen as the supraorbital artery. 2. Frontal, which in the same way goes

through the anterior supraorbital foramen; immediately after its origin it usually gives off the well-developed anterior ethmoidal artery, which goes through the ethmoidal foramen into the nasal cavity. 3. Muscular branches to the eye muscles.

"The superior ophthalmic artery is but little developed. It runs forward to the optic foramen, and goes through this on the under and lateral side of the optic nerve into the orbit, winds under the nerve to its anterior side, and anastomoses with the inferior ophthalmic artery. It gives off the ciliary arteries and the central artery of the retina." (*Loc. sup. cit.*, pp. 185, 186.)

In two of the dissections I have been unable to trace any anastomosis between the two ophthalmic arteries in the situation here described. In both these cases the anastomotic branch between the internal carotid and the internal maxillary was present. In two others this anastomotic branch was also present, and in these the superior ophthalmic artery was very small.

In the dog the carotid artery gives off as its first branch a thyroid artery. This in all the dissections has been the superior, but Ellenberger and Baum say that occasionally the inferior thyroid may also arise from the common carotid immediately after its origin. A muscular branch to the sternomastoid usually arises at about the same level as the thyroid. A little higher the ascending pharyngeal and the laryngeal arise. The artery now divides into the internal and external carotids. The internal carotid is always the first postero-external branch. It takes origin just at the level of the hypoglossal nerve. It is most easily reached in the living animal by retracting the common carotid outwards and tracing up its inner side. There is always present an enlargement close to its origin, which may possibly represent a carotid gland. The artery runs straight up with the vagus to the bulla, and enters the skull through the carotid foramen. It gives no branches in the neck. The external carotid gives as its first branch on the outer side the occipital. This artery

arises close to the internal carotid, and is of about the same size. In the living animal it may readily be mistaken for it. It is somewhat more superficial in origin, and will usually be found to give an anterior branch soon after its origin. The next branch and one of the largest is the lingual. Then comes the external maxillary, from which is derived the facial. The artery then breaks up into the superficial temporal, auricular, and internal maxillary arteries. The internal maxillary winds round the maxillary joint over the bulla, enters the pterygoid canal, and ends after leaving this by dividing into the infraorbital and palatine branches. Its branches may be divided into two sets, those given off before it enters the pterygoid canal, and those given off after it leaves it. The first set comprise the middle meningeal, the deep temporals, the inferior alveolar, and the muscular. The second set comprise a further set of muscular branches and the inferior ophthalmic.

Up to the point of origin of the ophthalmic arteries the dissections have corresponded with the description of Ellenberger and Baum, whose nomenclature I have followed. As some differences of detail have been noticed in the origin and communications of the ophthalmic arteries, it seems advisable to give their account in greater detail.

"The ophthalmic artery springs from the internal maxillary after it has left the pterygoid canal, and next runs between the periorbita and the temporal muscle, and further in on the orbital part of the frontal bone on the outer side of the periorbita to the ethmoidal foramen. Through this it runs into the skull as the ethmoidal artery. Shortly after its origin it, or one of its muscular branches, gives an anastomotic branch, which goes to the internal carotid. This, according to Bellarminow, who calls it the internal ophthalmic artery, gives off the central artery of the retina. The ophthalmic artery has the following branches :—

"1. Two muscular branches for the eye muscles, from one of which the rectus lateralis and superior, the periorbita orbital fat and tear glands are chiefly supplied; from the

other the rectus medialis and inferior and the obliquus lateralis. Both often arise from a common stem. They anastomose with the frontal artery and the malar branch. From them small branches run to the bulb and perforate the sclera as the anterior ciliary arteries.

"2. The lacrymal artery, which accompanied by the nerve of the same name runs on the rectus lateralis, and divides into branches to the lacrymal gland and upper lid.

"3. The frontal artery. This runs laterally on the superior rectus, and supplies this muscle, the rectus medialis, the obliquus lateralis, the orbital fat, and the periorbita, and reaches to the upper lid and lateral canthus, where it anastomoses with the superficial temporal.

"4. The posterior ciliary arteries—two arteries which accompany the optic nerve and by anastomotic branches form a network on it. At the entrance of the nerve into the bulb the two arteries form a ring on the sclera. From this ring on each side spring one long posterior ciliary and numerous short posterior ciliary arteries.

"5. The posterior ethmoidal artery. This runs into the skull through the posterior ethmoidal foramen, and then divides into two branches. These give off the anterior meningeal arteries, which anastomose with the arteries of the corpus callosum. They then leave the skull through the anterior ethmoidal foramen, and anastomose with the palatine and septal arteries." (*Loc. sup. cit.*, p. 186.)

In addition to this description there is given in small print, after the chapter dealing with the eye, the following account of Bellarminow's description of the ophthalmic arteries. "Bellarminow describes an external ophthalmic artery which rises from the internal maxillary artery and an internal ophthalmic artery from the internal carotid—(it is this which we have described as the ramus anastomoticus). The latter, much the smaller, gives off the central artery of the retina. The former, running nasalwards, divides into the medial iris artery, and a branch which, after reinforcement by one from the internal ophthalmic artery, becomes the

lateral iris artery. Forward in the choroid is formed an arterial ring, which is supplied by both iris arteries directly and indirectly through the mediation of the *circulus iridis major*, as well as by the choroidal arteries. From this branches are sent to the ciliary body and choroid."

In none of my dissections has this arrangement been exactly followed. In all of them the anastomotic branch from the internal carotid has entered the internal maxillary immediately before the origin of the inferior ophthalmic artery, and this latter has in all been represented by two separate branches. In consideration of the conditions found in the rabbit it is wiser to adhere to the terms superior and inferior, although Bellarminow's division into internal and external has the advantage of indicating their source from the internal and external carotids respectively. In only half the dissections has there been present a superior ophthalmic artery arising from the *ramus anastomoticus*. In the remaining half this artery has been derived from the internal carotid after the main trunk has left the internal carotid, and has entered the orbit through the optic foramen. The anastomotic branch is always of very fair size, and arising immediately after the internal carotid has reached the cavernous sinus, passes through the *fissura orbitalis* below the first division of the fifth nerve. In two dogs a large meningeal branch has arisen from the *ramus anastomoticus* on both sides. This branch has apparently taken in these cases the place of the middle meningeal.

If the anastomotic branch always supplied the interior of the eye it is certainly of sufficient size to maintain the circulation, and, as blood reaches it equally from the internal maxillary and internal carotid, it is probable that the supply to the eye would not suffer from the loss of only one of these sources. This, however, as has been shown, is not invariably the case. But in those cases in which the ciliary arteries and the central artery of the retina have been derived from a superior ophthalmic artery arising from the internal carotid, a free anastomosis has always been present between this

superior ophthalmic artery and one of the branches of the inferior ophthalmic artery. It is then, even in these cases, anatomically possible for the intraocular circulation to be maintained in the absence of one or other of the ophthalmic arteries.

In man a very different supply obtains. The anastomoses between branches of the ophthalmic artery and those of the external carotid are both few and far between. I will briefly enumerate them, taking as authority Quain's Text-book of Anatomy.⁽³⁾

The branches of the human ophthalmic artery with their anastomoses are there enumerated as follows (*loc. sup. cit.*, p. 408):—

1. The central artery of the retina usually arises in common with the internal ciliary trunk, sometimes with the external. No anastomoses.

2. Ciliary arteries: A, posterior from ophthalmic; B, anterior from muscular and lacrymal. The former have no anastomoses, and the latter no direct one.

3. Lacrymal. This anastomoses with the anterior deep, temporal, and transverse facial, and through the outer end of the sphenoidal fissure with the middle meningeal.

4. Recurrent branch to anastomose with internal carotid.

5. Muscular branches. Some anastomoses between the infraorbital and these branches must take place in the substance of the inferior oblique, but are not directly mentioned.

6. Supraorbital. This anastomoses with superficial temporal.

7. Anterior and posterior ethmoidal. No anastomoses given.

8. Palpebrals. No anastomosis given.

9. Nasals. Anastomose with facial.

10. Frontals. No anastomosis given.

The following variations are also enumerated. The ophthalmic artery may enter the orbit through the sphenoidal fissure. The lacrymal artery not infrequently, and, in rare cases, a large part, or even the whole of the ophthalmic artery

itself, arises from the middle meningeal. The lacrymal artery may also be reinforced by the anterior deep temporal artery. The ophthalmic artery has been seen to give off the middle meningeal.

Fr. Meyer,⁽⁴⁾ in discussing a case in which an abnormal course of the branches of the ophthalmic artery led to free arterial bleeding, and in which a subsequent post-mortem examination showed that the lacrymal and frontal arteries were derived by a common stem from the middle meningeal, sums up the literature of the subject and enumerates the possible varieties. There is, however, no mention made of the morphology. In view of the conditions found in the animals now under discussion, the occasional origin of the ophthalmic artery, or of some of its branches, from the middle meningeal, may be of morphological importance.

NOTE ON THE VENOUS RETURN OF THE BLOOD FROM THE EYE IN THE DOG.

The blood from the interior of the eye is mainly carried off by the vortico-se veins, a small quantity also escaping through the anterior ciliary veins and the central vein of the retina. The vortico-se veins are generally four in number, which ultimately unite to form two main trunks. The inferior and external one joins the ophthalmo-cerebral or inferior ophthalmic vein. The superior and mesial trunk runs into the cerebro-facial or superior ophthalmic vein. The two ophthalmic veins communicate with each other in the back part of the orbit and run into the cavernous sinus. The inferior one usually also communicates with the tributaries of the internal maxillary vein. Both veins receive numerous tributaries from all the structures in the orbit. The superior vein at the inner canthus joins the nasal veins and becomes the superficial facial. The inferior vein runs under the external wall of the orbit, and at the anterior border of the masseter joins the superficial facial to form the common facial trunk. It receives muscular branches from

the temporal and masseter, and communicates with the internal maxillary. After the common facial has received the lingual it is known as the external maxillary, and this vein is joined by the internal maxillary to form the external jugular. Soon after its formation this vein sends a large communicating branch across the middle line to its fellow of the opposite side, and terminates by joining the internal jugular near the first rib. The blood from the cerebral sinuses is mainly carried off by three veins, the external and internal jugulars and the vertebral. Of these three the latter is said to be the more important. The two former vary reciprocally. The external being in most cases the largest. The internal jugular has a large communication with the vertebral vein immediately after its exit from the skull. A coarse injection, such as plaster of Paris, if injected into the external jugular vein, fails to reach the facial owing to the valves. There does not, however, appear to be anything to prevent it reaching the cerebral sinuses, and so the ophthalmic veins. If it is desired to make an injection of the facial veins, it is best to employ hot gelatine and inject through the carotid artery. The accompanying diagram will serve to show how extremely free the venous outflow from the eyeball really is.

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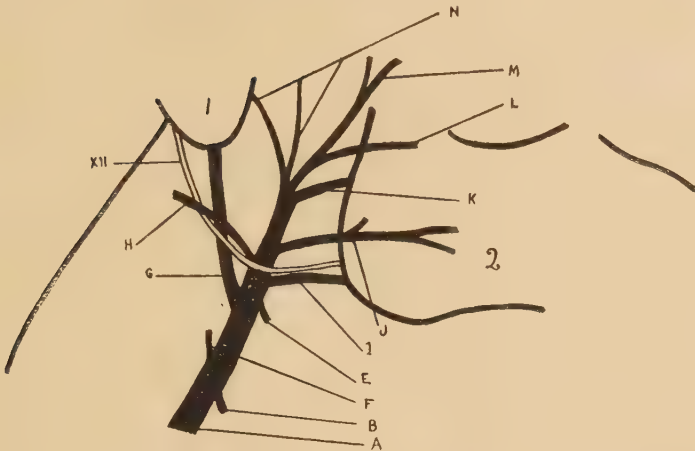


FIG. 1.—Scheme of the carotid arteries in the rabbit:—A, common carotid artery; B, thyroid artery; E, laryngeal artery; F, ascending pharyngeal artery; G, internal carotid artery; H, occipital artery; I, lingual artery; J, external maxillary artery; K, internal maxillary artery; L, transverse facial artery; M, superficial temporal artery; N, auricular artery. Hypoglossal nerve. 1, placed on the bulla tympani; 2, on the lower jaw.

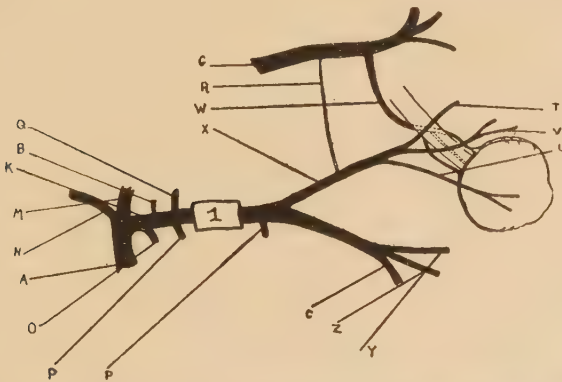


FIG. 2.—Scheme of the internal maxillary and ophthalmic arteries of the rabbit:—A, external carotid artery; B, tympanic artery; C, superior alveolar artery; G, internal carotid artery; K, internal maxillary artery; M, superficial temporal artery; N, auricular artery; O, inferior alveolar artery; P, muscular arteries; Q, middle meningeal artery; R, ramus anastomoticus; T, ethmoidal artery; U, lacrymal artery; V, frontal artery; W, superior ophthalmic artery; X, inferior ophthalmic artery; Y, infraorbital artery; Z, pterygopalatine artery. 1, placed on the pterygoid canal.

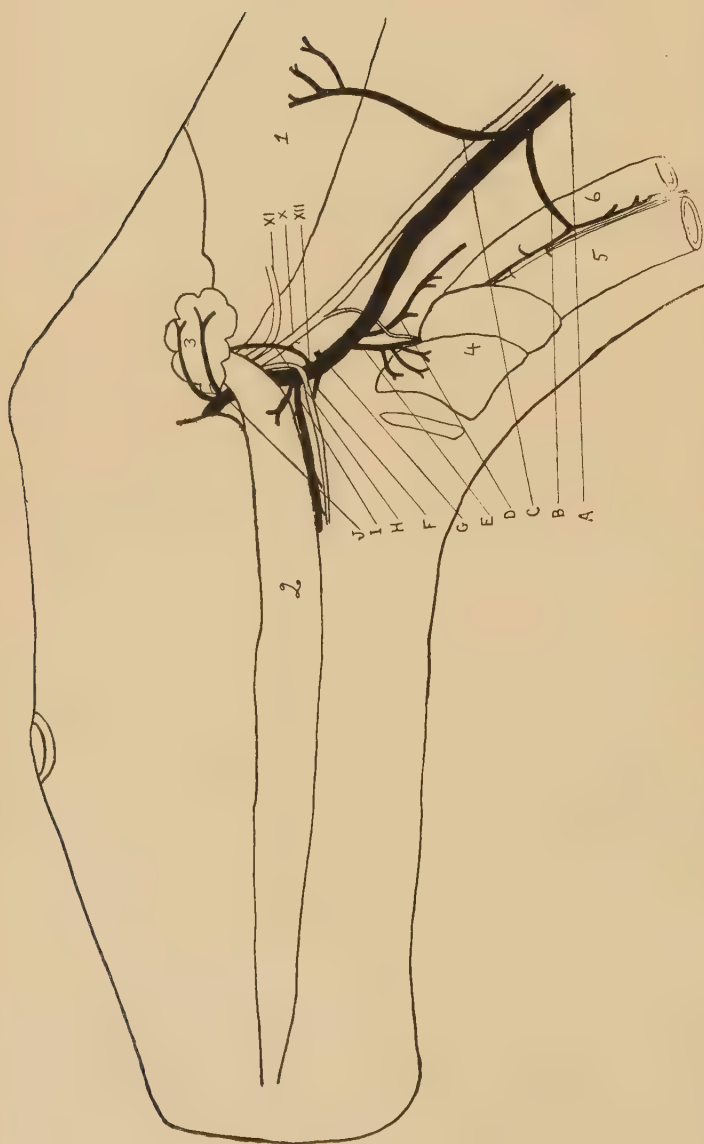


FIG. 3.—Scheme of the carotid arteries in the dog :—A, common carotid artery; B, thyroid artery; C, muscular branch to sternomastoid; D, muscular branch to deep neck muscles; E, laryngeal artery; F, ascending pharyngeal artery; G, internal carotid artery; H, occipital artery; I, lingual artery; J, external maxillary artery; X, XI, XII, vagus, spinal accessory, and hypoglossal nerves. 1, placed on the sterno-mastoid; 2, on the digastric; 3, on the salivary gland; 4, on the larynx; 5, on the trachea; 6, on the oesophagus.

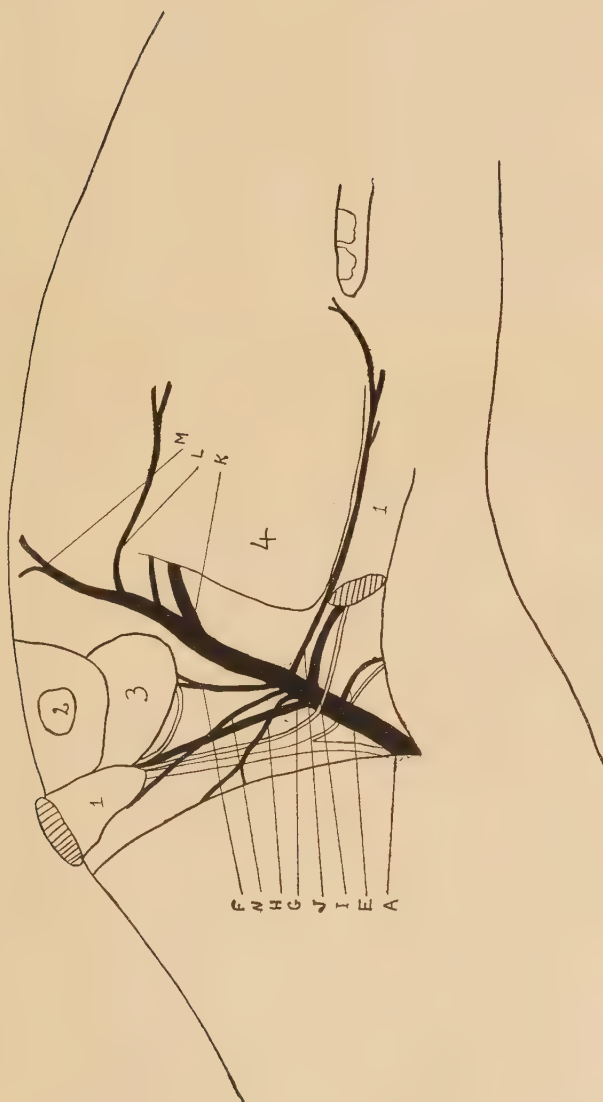


FIG. 4.—Scheme of carotid arteries in the dog, traced higher after division of the digastric:—A to N as in Fig. 3.
1, placed on the digastric; 2, on the ear; 3, on the bulla tympani; 4, on the lower jaw.

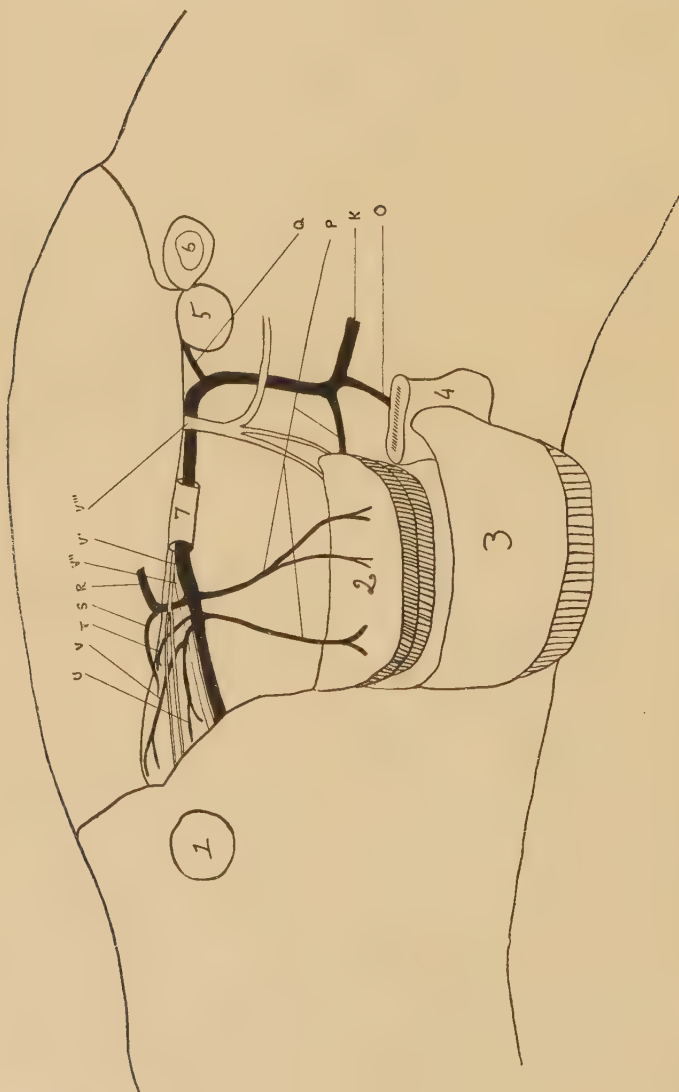
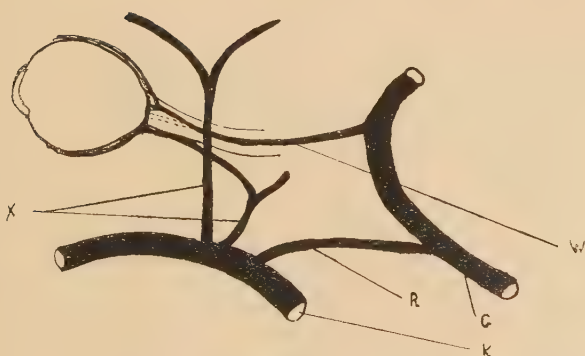
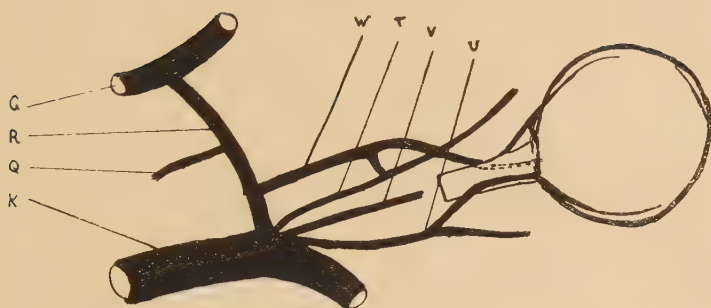


FIG. 5.—Scheme of internal maxillary and ophthalmic arteries in the dog:—K, internal maxillary artery; O, inferior alveolar artery; P, deep temporal artery; Q, middle meningeal artery; R, ramus anastomoticus; S, superior ophthalmic artery (inferior of Bellarminow); T, ethmoidal artery; U, lacrymal artery; V, frontal artery. V'V''V''', the three parts of the fifth nerve. 1, placed on the eye; 2, on the temporal and pterygoid muscles, cut and turned down; 3, on the masseter, also turned down; 4, on the lower jaw; 5, on the bulla tympani; 6, on the ear; 7, on the pterygoid canal.



FIGS. 6, 7, and 8.—These represent variations in the orbital arteries in the dog:—G, internal carotid; K, internal maxillary artery; Q, middle meningeal artery; R, ramus anastomoticus; W, superior ophthalmic artery; X, inferior ophthalmic artery; T, ethmoidal artery; U, lacrimal artery; V, frontal artery.

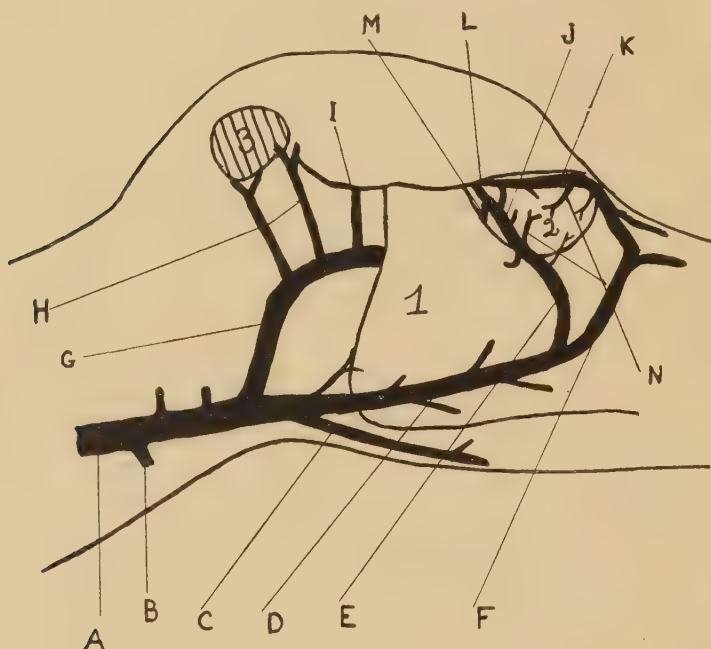


FIG. 9.—Scheme of the external jugular and ophthalmic veins in the dog ; the eyeball, margin of the orbit, and masseter have been removed:— A, external jugular vein ; B, communication to external jugular of the opposite side ; C, lingual ; D, common facial ; E, deep facial ; F, superficial facial ; G, internal maxillary ; H, auricular ; I, to lateral sinus ; J, inferior ophthalmic or ophthalmocerebral vein ; K, superior ophthalmic or cerebro-facial vein ; L, to cavernous sinus ; M, to infraorbital vein ; N, vorticose veins. 1 is placed on the inferior maxilla ; 2, on the floor of the orbit ; 3, on the ear.

ON THE RELATIONS BETWEEN INTRAOCULAR TENSION AND THE GENERAL BLOOD-PRESSURE.

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IN bringing forward these experiments, we do not propose to discuss the results obtained by earlier observers, as many of these are contradictory, owing to faulty methods and other causes. Our experiments most accurately conform to those of von Schultén* and Bellarminow,† although, as will be seen later, the method they employed is open to criticism.

Method.

About 40 experiments have been performed—upon dogs and a few cats. The animals were anæsthetised with morphia and A.C.E. mixture: in most cases they were also curarised. The blood-pressure was usually taken from the femoral artery, occasionally from the carotid on the opposite side to the eye which was being observed.

The apparatus used for the measurement of the intra-ocular tension consisted of a cannula (A), a fine-bored glass tube (B), a manometer, and a pressure bottle (Fig. 1). The cannula (A) is a modified form of Leber's intraocular pressure cannula, and is the same as that used by Starling and Pflüger for determining the rate of flow of the aqueous secretion. It consists of a gilt hollow needle, having two small lateral openings at *a* and *b* upon opposite sides near the pointed end, which is also open. This ensures free communication with the interior of the eye. The distal end, *c*, is closed by a plug, which can be replaced by a straight wire

* V. Schultén, Arch. f. Ophth., vol. xxx, part 3, p. 1, 1884.

† Bellarminow, Pflüger's Archiv., vol. xxxix, 1886; Annales d'Oculistique vol. xevii, p. 181.

for cleaning out any clot or other obstruction. A side tube, *d*, near the distal end, leads off to the manometer by means of two fine-bored glass tubes, *e* and *B*, connected by india-

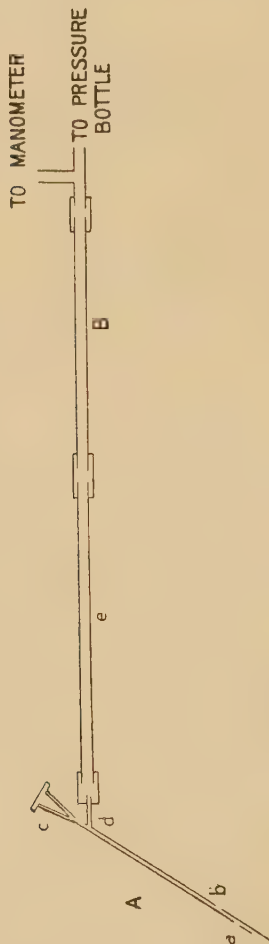


FIG. 1.

rubber joints. The tube *e* is not essential, but is inserted for convenience. The flexible joints allow a limited amount of mobility for the necessary manipulations; they are made as

little elastic as possible by bringing the glass tubes nearly into apposition, and using thick-walled pressure tubing for the junctions. A glass T-tube connects B with the manometer and the pressure bottle.

The manometer used for obtaining graphic records was either a Hürthle manometer, provided with a thin rubber membrane, or an ordinary Marey tambour, about twice the diameter of the Hürthle, with a rather thicker membrane. In most of the experiments only qualitative changes were observed, so that it was unnecessary to calibrate the manometer. In a few cases in which absolute measurements were taken, it was simpler and more accurate to use a fine-bored mercury manometer.

In many of the earlier experiments which were performed by one of us (J. H. P.), the cannula was inserted into the vitreous chamber of the eye. When this method worked well, it gave as conclusive results as in the later experiments, in which the cannula was inserted into the anterior chamber. The former method, however, is not so reliable as the latter, owing to the consistency of the vitreous, which often prevents a free to-and-fro movement in the cannula, and may cause a valvular effect. It is of interest as demonstrating the identity of the results obtained from the two chambers, but those obtained from the anterior chamber are generally the more reliable. Hence it was considered advisable to repeat the experiments of v. Schultén and Bellarminow, in which the cannula was placed in the vitreous.

A further modification of all previous experiments was also introduced. It has been considered essential that no fluid should either leave the eye or enter it when the cannula is inserted. It is, however, quite impossible to accurately foretell the intraocular pressure before inserting the cannula. In our experiments, the whole apparatus was filled with normal saline solution; the pressure bottle was raised to about the pressure anticipated, and the cannula was introduced whilst the fluid was flowing from it. It is very

important that the cannula be perfectly sharp and smooth, so that it may be pushed across the anterior chamber very quickly, otherwise the aqueous escapes, and the iris and lens are wounded and block the apertures in the cannula. Immediately after the cannula is inserted, an air bubble is let into the tube B. The pressure bottle is then raised or lowered according to the movements of the bubble. In a few minutes it assumes a mean position, varying only in accordance to the transmitted cardiac and respiratory waves.

Results.

In determining the effects of changes in the general blood-pressure, it is first necessary to eliminate other possible sources of variation in the intraocular tension. Of these, the most important are the effects of contraction of the extrinsic and intrinsic muscles of the eye. The former consist of two groups—the striated and the unstriated. Contraction of the extrinsic striped muscles, closure of the lids, &c., produce marked changes in the intraocular tension. It is therefore necessary to fully curarise the animal. The extrinsic unstriated muscles have been found to be without effect in the dog, though they are a source of error, as will be mentioned later, in the cat. Movements of the intrinsic muscles of the eye produce no effect upon the intraocular pressure; or, if any, it is too slight to be manifested by the methods employed. Thus the effects obtained in various ways with and without complete paralysis of the iris and ciliary muscles by atropin are identical.

Cervical Sympathetic.—Stimulation of the peripheral end of the cervical sympathetic was investigated in the cat. It was invariably followed by a considerable rise in intraocular pressure, irrespective of any change in the general blood-pressure. This confirms the results obtained by Adamük, v. Hippel, and Grünhagen, &c. It is not due, however, to vascular changes occurring in the eye. It is not due to movements of the iris, since it occurs after prolonged instil-

lation of atropin previous to the operation, and also after large intravenous injections of atropin, sufficient to abolish inhibition of the heart on strong stimulation of the vagi. It was finally proved not to be due to vascular changes, since it occurred for a considerable period after the death of a curarised cat, and is therefore undoubtedly due to pressure exerted upon the globe by the contraction of unstriped muscle contained in the orbit and innervated by the cervical sympathetic. It is therefore impossible to demonstrate by this method any changes in the intraocular vessels by stimulation of the cervical sympathetic. This fact vitiates all Bellarminow's results, which were obtained from cats.

Vth Cranial Nerve.—Stimulation of the peripheral end of the Vth nerve has been without effect, except when a simultaneous rise of blood-pressure occurred, probably from spread of current to meningeal sensory nerves, still connected with the brain. The manometer is probably not sensitive enough to record the variation due to local dilatation, if this occur.

Changes in the Blood Supply of the Eye.—In lower mammals (dog, cat, &c.) the intraocular blood supply is derived almost entirely from the internal maxillary artery, which forms the termination of the external carotid.* In the dog, there is a large anastomotic branch from the internal carotid within the skull, which usually joins the internal maxillary just before the ophthalmic artery or arteries are given off. Tying the external carotid, therefore, cuts off the main blood supply to the eye. In spite of the slight rise in general blood-pressure which this operation causes, there is invariably a well-marked fall in intraocular tension. Ligature of the internal carotid, which is much smaller than the external, causes no change in intraocular tension if the external is still patent. If the external carotid is tied, although the intraocular tension falls, and remains subnormal for a considerable period, the eye is still well supplied with blood, through the internal, by its anastomotic

* *Vide Henderson, ante p. 260.*

branch, and through circle of Willis; so that changes in the general blood-pressure still affect the eye.

Ligature of the common carotid of the opposite side causes no effect.

Changes in General Blood-Pressure.—The intraocular tension responds passively to all variations in the general blood-pressure. This is the case also if the external carotid is tied, or if the skull is freely laid open.

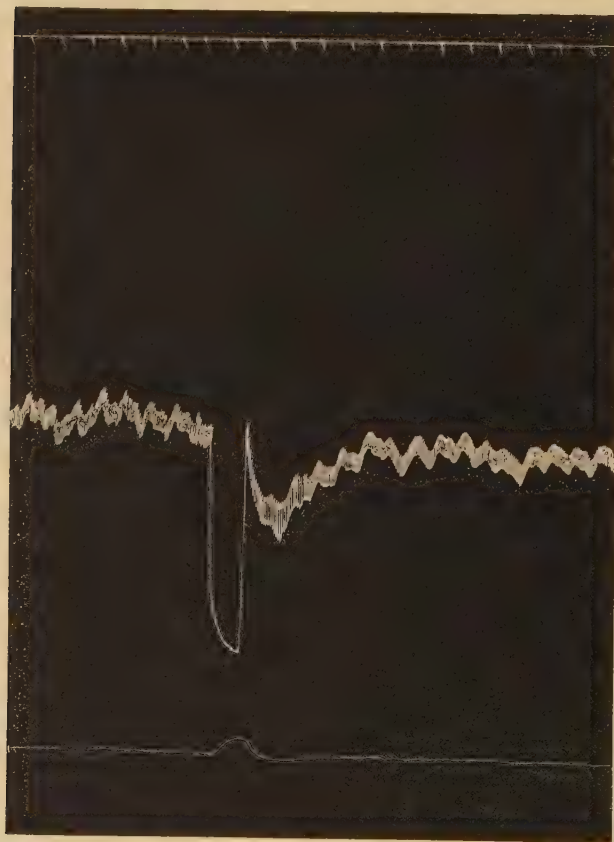


FIG. 2.—Dog. Morphia, A.C.E. and curare. Femoral blood-pressure. Compression of thoracic aorta. Time in 10 sec. intervals.

The respiratory and cardiac oscillations are usually clearly represented upon the air bubble in the tube B: they are not recorded by the manometer. The general curve of

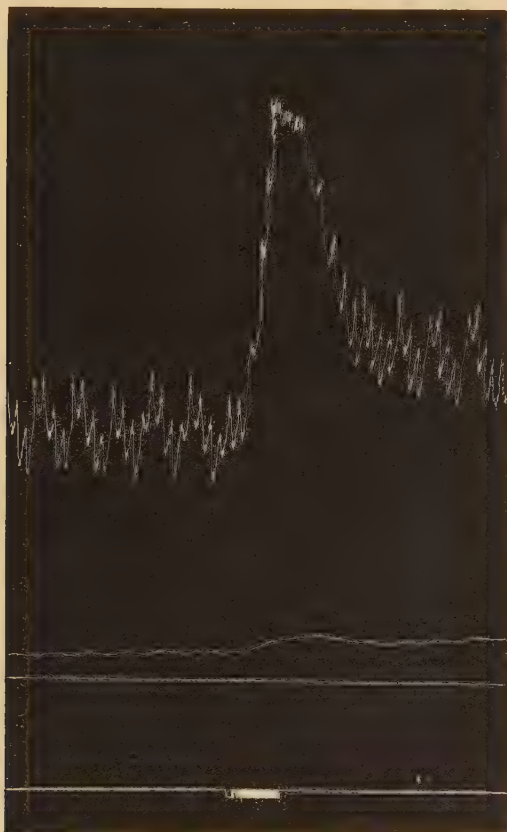


FIG. 3.—Dog. Morphia, A.C.E. and curare. R. carotid pressure; L. intraocular pressure. Traube-Hering curves: stimulation of vaso-motor centre.

the blood-pressure is reproduced by the intraocular manometer, but, as it were, damped. There is a short latent

period (1—2 sec.), the changes are slower, and the curve flatter.

The blood-pressure has been varied by the following means.

(a) *Mechanical*.—Rise of blood-pressure in the anterior part of the body has been brought about by compression of the abdominal or thoracic aorta. It is accompanied by a passive rise of intraocular tension.

(b) *Stimulation of Nerves*.—Stimulation of the central end of sensory and mixed nerves (*e.g.*, sciatic) causes rise in both. The central end of the vagus has always given us a pressor effect, accompanied by rise in eye-tension. Cardiac inhibition through the peripheral end of the vagus causes a sharp fall in intraocular pressure. The rise in blood-pressure by stimulation of the vaso-motor centre, peripheral cut end of cervical cord, or splanchnic nerves, causes the usual passive effect. Traube-Hering curves are accurately reproduced.

(c) *Drugs*.—Adrenalin, nicotin, strychnin, pilocarpin, quinin, amyl nitrite and large doses of chloroform give results in accordance with their effects upon the blood-pressure. It may be noted that pilocarpin apparently has no specific secretory effect. We have not been able to obtain any local vaso-constrictor effect by injecting adrenalin into the common carotid artery.

(d) *Asphyxia*.—The rise in blood-pressure due to asphyxia is accompanied by a corresponding rise in intraocular tension, which continues during the fall in blood-pressure. This is doubtless due to the obstruction to the return of venous blood to the heart in this stage.

(e) *Death*.—The normal intraocular pressure of the dog varies from 20 to 30 mm. Hg. After death it gradually and very slowly falls to zero.

We have done some experiments in which the intracranial pressure has been raised by various means. If air is pumped into the cranium, the animal soon dies from absorp-

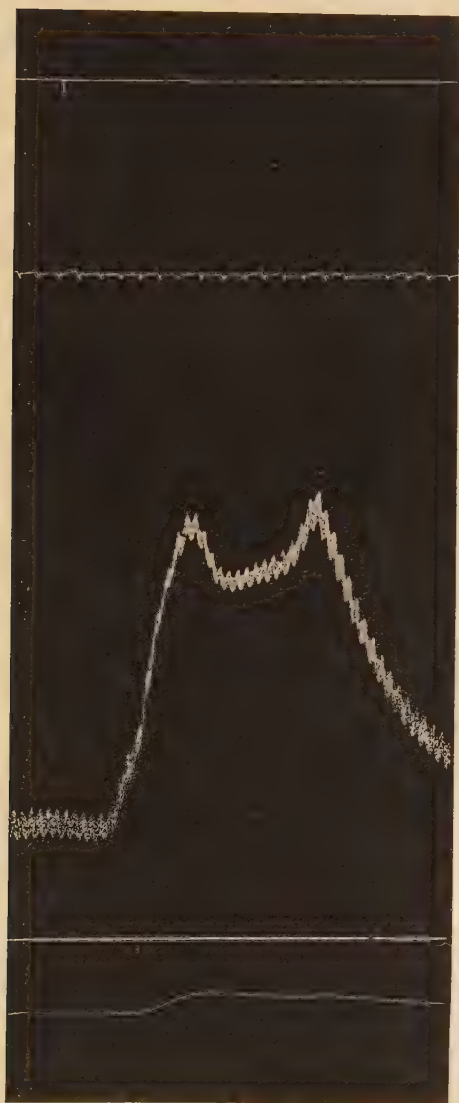


FIG. 4.—Dog. Morphia, A.C.E. and curare. Femoral blood-pressure; external carotid tied. 1 minim of 5 per cent. solution of nicotin injected into femoral vein. Time in 10 sec. intervals.

tion of air into the circulation. Under these circumstances the intraocular pressure rises enormously, owing to the same cause as in the later stages of asphyxia, but the effect is much more marked.

Remarks.

In interpreting the results obtained by the manometric method upon the eye, we have to consider—apart from the accuracy of the method itself—(1) the elasticity of the coats of the eyeball, (2) vaso-motor changes, (3) the secretion of intraocular fluid.

Koster Gzn,* experimenting upon excised eyes, showed that, under low pressures, up to 100 mm. Hg, the energy is expended in altering the shape of the eye, so that it tends to assume a spherical form; whilst it is only under pressures above 100 mm. Hg, that the elasticity of the sclerotic becomes the essential factor. Hence for the comparatively small variations at low pressures now under consideration, we may ignore the elasticity of the sclerotic.

As regards the secretion of intraocular fluid, Starling and Pflüger have shown in some experiments which will be published shortly, that the secretion follows the physical laws of filtration. In any case, it is improbable that active secretion is so rapid as to affect much the intraocular tension during the comparatively rapid changes brought about in these experiments.

Consequently, the variations observed may be regarded as due to changes in the volume of the intraocular blood-vessels: even if slight changes in secretory activity occur they will be in the same direction, constriction of arterioles being associated with diminished, and dilatation with increased secretion. The evidence of active vaso-motor changes in the eye have hitherto depended entirely upon ophthalmoscopic

* Koster Gzn, Arch. f. Ophth., vol. xli, part 2, p. 141, 1895; vol. lii, part 3, p. 402, 1901.

observations, which are open to grave doubt. We have ourselves failed to demonstrate such changes by the present method; but the experiments afford ample evidence of passive vascular changes.

The expenses of this research were defrayed by a Royal Society grant.

METASTATIC CARCINOMA OF THE CHOROID.

By J. HERBERT PARSONS, *Curator*.

THE following are the detailed clinical and pathological notes of the case of metastatic carcinoma of the choroid referred to by Mr. Holmes Spicer on p. 235 of the Transactions of the Ophthalmological Society of the United Kingdom, vol. xxii, 1902 :—

The patient was a lady, æt. 37, unmarried. Her right breast was removed in 1899 for scirrhus, a large area of skin and some axillary glands having been taken away at the operation. The patient enjoyed good health afterwards until May 14th, 1902, when she consulted Mr. John Couper on account of dimness of vision in the L. eye, noticed a few days previously. V. in this eye, after correction of slight hypermetropic astigmatism = bare 6/9, J 1 slowly, R. V. corrected = 6/4, J 1.

L. Ophthalmoscopic Examination.—Media clear = growth clearly seen as an opaque detachment up and in from the disc. Some of the adjoining retina below was detached in broadish folds, and had remained more or less transparent, as did the fluid between it and the choroid. There was nowhere any trace of hæmorrhage visible.

Later on the same day a consultation was held with Mr. Howard Marsh, and on the following day with Mr. Holmes Spicer.

The eye was enucleated on May 16th, 1902.

[I am indebted for the clinical notes and permission to publish the case to Messrs. John Couper and Holmes Spicer.]

PATHOLOGICAL EXAMINATION.—The eye was placed in 10 per cent. formol immediately after excision. After a few days it was frozen, and bisected sagittally with a slight inclination down and out.

Macroscopic Examination.—Cornea, a.c., iris and lens normal. Retina detached widely below, with albuminous coagulum in



FIG. 1. $\times 4$.

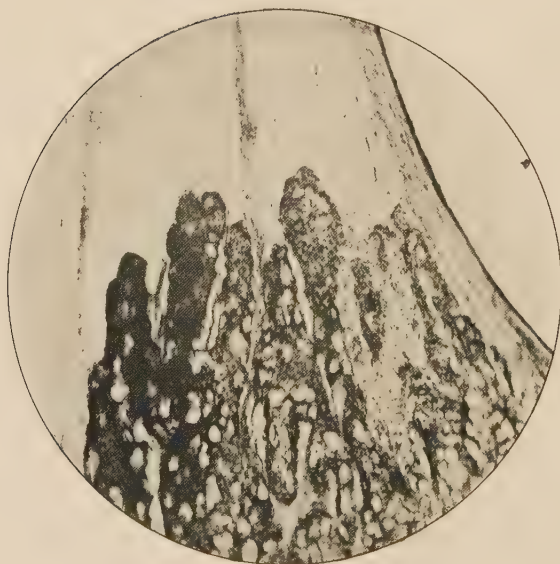


FIG. 2. $\times 60$.

PARSONS—Metastatic Carcinoma.

the sub-retinal space. Above it is still in apposition to the growth. Choroid shows large thin whitish growth, extending forwards from the disc to the equator. It is barely 2 mm. thick in its thickest part, which is near the front. It extends over a large area of the choroid.

Microscopic Examination.—Cornea, a.c., iris and lens normal. The retina is detached widely below, but is adherent to the growth, except over its peripheral half, where it is detached. (The latter may be an artefact.) The growth extends widely over the lower side, starting from the edge of the disc. There is also a patch, 4 mm. broad by 1 mm. thick in the thickest part, situated above the disc. It also invades the lower part of the nerve, extending for about 1 mm. behind the lamina cribrosa. (Fig. 1.)

The growth consists of spheroidal epithelial cells, many of which have dropped out, whilst many others appear vacuolated. They have an alveolar arrangement, and there is no stroma between the individual cells. The alveoli form spaces bounded by the separated fibres of the choroid. At the anterior edge the phalanx of columns of the growth advancing between the planes of the choroidal stroma is particularly striking (Fig. 2). Minute outlying nodules are seen, few in number, in the sclerotic.

The growth is a glandular carcinoma. It contains less fibrous tissue than the primary scirrhus contained (presuming it to have been a typical example). This is not unfrequent in metastases.

REMARKS.

This is a typical metastatic carcinoma of the choroid derived from a primary growth in the most common situation.

In the discussion upon Mr. Rockliffe's case (Trans. Ophth. Soc., vol. xxii, p. 236, 1902), Dr. Hill Griffith called attention to the flatness of these tumours as compared with primary sarcomata of the choroid. Mr. Devereux Marshall remarked that "sarcomata, if seen early enough, were doubtless flat." I do not think that this statement is

generally true, if by "flatness" we understand a large difference between length and thickness. This is universal in metastatic carcinomata of the choroid at all stages of their growth. It is only rarely the case in sarcomata, such growths having been described in German ophthalmic literature as "Flächensarcome." They are extremely rare—only one example having been recorded in the pathological reports of this hospital. They are allied to the Annular Sarcomata ("Ringsarcome") of the ciliary body, an infiltrating type of growth, of which I am describing a good example in a forthcoming number of Graefe's Archiv für Ophthalmologie. The ordinary primary sarcoma of the choroid, even from the earliest stages observed in typical examples, is lenticular in shape, and therefore cannot be accurately described as flat.

The shape of these tumours is more important than might appear at first sight, since it indicates fundamental differences of origin and growth. The ordinary primary sarcoma starts in the actual stroma cells of the choroid itself. Following the laws of growth, the cells proliferate in the directions of least resistance. Since the growth commences *in* the actual tissues themselves, the resistance is equal in all directions at first, so that at this stage we might expect the tumour to be spherical; such an early stage, however, has never been described. Soon the greater resistance on the side of the sclerotic makes itself felt, the advance is less in this direction, whilst equal in other directions; hence the tumour becomes roughly elliptical, growing twice as fast laterally as in thickness. This mode of advance continues until the membrana vitrea is burst through, which results from equable stretching rather than from any localised attack by the growth upon any one spot. At the hole in Bruch's membrane, which is necessarily central as to the surface of the tumour, resistance is greatly relieved; proliferation becomes most active in this direction, and a new focus is established in the sub-retinal space. Here again resistances are equalised, growth proceeds equally in

all directions, and the very characteristic globular head of the tumour is formed, connected with the main mass by a short neck at the level of Bruch's membrane.

The commencement and sequence are quite different in the case of metastatic carcinomata of the choroid. Metastasis here can only occur through the blood-vessels, since it is inconceivable that deposits can be brought from the breast, for example, by way of lymphatics. The frequent affection of both eyes is almost conclusive as to a blood-vascular origin. The earliest focus must be of the nature of an embolus, probably in the finer arterioles of the choroid, The vessel affected is blocked, the cancer cells proliferate, and burst through, or replace the walls of the vessel. They are now situated in the lymph-spaces in the choroid, which lie directly outside the blood-vessels. Hence they lie *between* the planes of the choroidal stroma. We know from the frequent cases of detachment of the posterior part of the ciliary body, that traction readily draws the planes of the stroma of the uveal tract apart, and that those which offer greatest resistance and persist longest are those which are more or less concentric with the curvature of the globe, those transverse or oblique to this direction being relatively feeble. The same is shown in the further growth of metastatic deposits. Lying as the cells now do between these concentric planes, the directions of least resistance are along them; hence most of the growth is lateral, a minimum increase of thickness taking place. The appearances shown in Fig. 2 are, to my mind, most striking, and afford overwhelming evidence of the accuracy of this view as to the mode of growth. Whether the same explanation applies to the rare "Flächensarcome" or not, the scantiness of the material makes it difficult to decide.

Of course, it is to be understood that these descriptions apply to the essential tendencies of growth in the given cases. These tendencies are often modified in detail, *e.g.*, by proximity to a vorticose vein, so that a new path of diminished resistance is open to the growth. Such modifi-

cations are usually obvious in individual cases, and do not affect the general statements made above.

Since the publication of Mr. Devereux Marshall's excellent paper on "Metastatic Carcinoma of the Eyeball" in an earlier number of these Reports (vol. xiv, pt. 3, p. 415,

No. of case.	Author.	Where published.	Sex.	Age.	R. or L.	V. and T.
25	Samelsohn ..	Berlin klin. Woch., 1891	F.	43	L.	—
26	De Schweinitz ..	Trans. Amer. Ophth. Soc., 1898, p. 313	F.	40	R.	V = fingers at 2 ft. Tn.
27	De Schweinitz ..	Ditto	F.	43	L.	V = 10/200
28	Von Michel ..	International Congress, Utrecht, 1899	F.	—	—	Tn. . . .
29	Rowan ..	Trans. Ophth. Soc. U.K., 1899	M.	55	L.	—
30	Lagrange ..	Tumeurs de l'œil, vol. i, p. 512	F.	48	R.	T + 1 ..
31	Lagrange ..	Ditto	M.	—	R.	—
32	Rockliffe ..	Trans. Ophth. Soc., 1902	F.	46	L.	V = p.l. .. Tn.
33	Parsons ..	Present paper	F.	37	R.	V = 6/6 .. Tn.
					L.	V = 6/9. .. Tn.

1897), 8 fresh cases have now been published; and another earlier case, which Mr. Marshall missed, brings the total number of cases up to 33, 41 eyes being affected.

The following table supplements Mr. Marshall's, and brings it up to date:—

Pathological examination of eyeball.	Seat of primary growth.	Seat of secondary deposits other than eye, and result of post-mortem, if obtained.	Duration of life after eye was first affected.	Remarks.
Flat tumour extending over disc, invading nerve. Extraocular tumour also	—	No autopsy.		
Flat tumour, extending over macular region nearly to equator	L. breast ..	? Intracranial and spinal.		
Flat tumour, extending over macular region, with red spots	L. breast ..	—	—	Clinical only.
Flat tumour over temporal side	Breast.			
Flat tumour, covering posterior pole	Lung.			
Flat tumour over whole temporal and half nasal areas, with growth at outer part of iris and in a.e.				
Intra- and Extra-ocular tumours. Intra-, pigmented anteriorly; extra-, quite white. 'Undoubted carcinoma.'				
Flat tumour over $\frac{3}{4}$ fundus, extending to ciliary body one side; O.N. involved.	R. breast ..	Pleurisy. Tumour in R. groin.	9 months.	
Not examined	—	No autopsy ..	—	Clinical only.
Flat tumour from disc to equator, up and in; small down and out; O.N. involved	R. breast.			

TWO CASES OF GUMMA OF THE CILIARY BODY.

By J. HERBERT PARSONS, *Curator*.

CASES of gumma of the ciliary body rarely become available for pathological examination. I have had the unusual opportunity of examining three very severe, apparently uncomplicated cases, recently. One of these is reported by Mr. Morton and myself in the last volume of the Transactions of the Ophthalmological Society (vol. xxii, p. 266, Plate xxii, Fig. 2). It was removed from the cadaver. The other two are recorded here; the disorganisation of the eyes was so great, and the pain so severe that it was considered advisable to excise them.

CASE I.

T. H., male, æt. 64.

3.vii.02. History of primary sore 3 months ago. Scaly papular rash on forehead, rupial on body.

L. eye. Chemosis: cornea hazy; iritis, posterior synechiæ.

17.vii.02. Lymph in a. c.; blood in substance of cornea; sclerotic bulged in two places below cornea by ? gumma.

24.vii.02. L. V. — bare p. l., projection bad.

30.vii.02. Yellowish projection from sclerotic in ciliary region below; exudation in lower part of a. c.

PATHOLOGICAL EXAMINATION.—The eye was hardened in 10 per cent. formol, frozen, and bisected in a sagittal plane.

Macroscopic Examination.—Cornea—surface rough, looks blood-stained. A. c.—full of exudate and blood. Sclera—perforated below by inflammatory mass, continuous with the ciliary body, and communicating with a. c.; the mass is 5 mm. thick in thickest part (Fig. 1). Lens—cataractous. Vitreous—filled with white filaments which radiate from the optic disc and also from the gumma. Retinal and choroid *in situ*.

Microscopic Examination.—Cornea—epithelium irregular, somewhat cedematous; Bowman's membrane intact; substantia

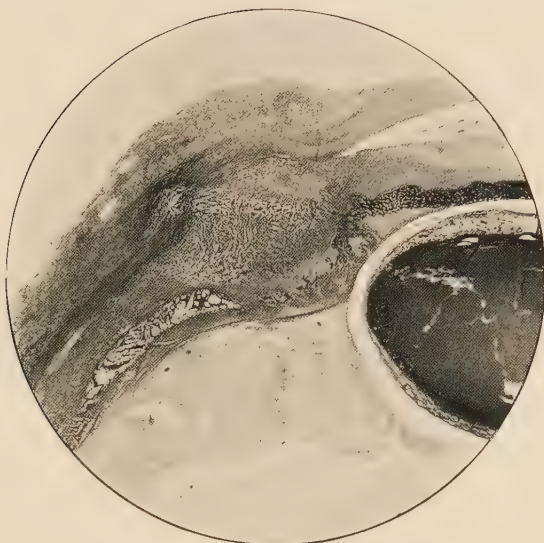


FIG. 1. $\times 6$.



FIG. 2. $\times 7$.

PARSONS—Gumma of Ciliary Body.



propria slightly infiltrated, especially at periphery; Descemet's membrane intact, endothelium mostly disappeared, the membrane being covered with red corpuscles and exudate. A. c.—full of fibrinous coagulum containing leucocytes and red corpuscles; the upper angle is blocked with fibrin and cells, canal of Schlemm being open; lower angle is full of fibrin, &c., continuous with iris tissue and ciliary body. Iris—much inflamed, swollen and infiltrated throughout, especially below, where it is filled with fibrin and inflammatory products, which are continuous with those in the a. c.; retinal pigment epithelium layer enormously thickened, especially below. Posterior chamber—full of fibrinous exudate. Ciliary body—inflamed and infiltrated with round cells above; below it is the seat of a necrosing granuloma, almost identical in every respect with that described by me in *Trans. Ophth. Soc. U. K.*, vol. xxii, p. 266 (with Plate xxii, Fig. 2). There is the same massing of inflammatory products of the same type, without giant-cells, accompanied by extensive necrosis and destruction of the sclerotic. Vitreous—pervaded by fibrinous inflammatory products, which especially surround the ciliary processes, the latter being almost depigmented. Lens—it is doubtful if the capsule is intact; cortical fibres are vacuolated; nucleus normal. Retina—much infiltrated and disorganised, the layers being differentiated with difficulty. Choroid—congested and inflamed.

CASE II.

C. G., female, æt. 25. L. eye quite normal 6 weeks ago; then became watery and slightly bloodshot. There was pain in the side of the face. Three weeks ago the inflammation increased, and the vision rapidly failed. The “staphyloma” was first noticed a week ago. The patient has been losing flesh for 6 weeks; no history of syphilis.

R. eye. Cornea clear. A. c. good. Iris and pupil normal. Fundus normal. V = 6/5. Tn.

L. eye. Intense injection. “Staphyloma” below cornea, containing ciliary body; sclerotic thinned here. Cornea hazy. A. c. shallow. Iris discoloured; pupil blocked, margin bound down to lens. No red reflex. V = hand shadows, projection bad. T slightly less than R.

On the following day the L. T = - 2, and it was noticed that the corresponding pre-auricular gland was swollen.

The eye was excised 5 days after first note.

PATHOLOGICAL EXAMINATION.—The eye was hardened in 10 per cent. formol, frozen, and bisected in a sagittal plane.

Macroscopic Examination.—Cornea hazy. A. c. of unequal depth; deeper below where the iris is retracted, shallow above, where the angle is blocked by adhesion of the iris to the back of the cornea for 3 mm. Iris—pupil very small, blocked; ring synechia; iris bombé above; in a condition of total posterior synechia below. Lens, *in situ*. Ciliary body—much thickened below; covered internally by dense white exudate, which stretches out into the vitreous; there is a brownish swelling outside in the situation of the “staphylomatous” condition: greatest thickness = 4.5 mm. (Fig. 2). Vitreous—full of exudates. Retina and choroid—*in situ*.

Microscopic Examination.—Cornea—epithelium and Bowman’s membrane intact and normal; substantia propria slightly infiltrated throughout; Descemet’s membrane normal above. A. c. —upper angle blocked by adhesion of iris to cornea for 3 mm.; lower angle widely open where the gumma invades a. c. Iris—intensely congested and inflamed throughout; bombé above—there are small dense aggregations of mononuclear leucocytes at the periphery in this part, and both the retinal and uveal pigment are much disturbed and have proliferated; adherent to lens over whole area below, with the intervention in places of leucocytes and low developed fibrous tissue. Ciliary body—congested above, and slightly detached in posterior part, where there is an albuminous coagulum in the subciliary space. Below it is the seat of a necrosing granuloma, which has broken through into the a. c. in front, and into the vitreous internally, so that it is in contact with the lens just in front of the equator. The ciliary processes are entirely disorganised, and are only represented by irregular wavy lines of persistent retinal pigment cells. The main mass is made up of badly staining leucocytes, which have run together into an albuminous mass, in which faint remnants of nuclei, red blood corpuscles, shreds of fibrous tissue and pigment granules can be seen. There are no giant-cells, and there is no effort towards repair. The sclerotic

has been destroyed for 3 mm., the lamellæ at its termination being spread out, and separated from one another by leucocytes. The external mass, which looked brown macroscopically, consists of intensely inflamed episcleral tissue. The blood-vessels are widely dilated and crammed with red corpuscles; the stroma is densely packed with mononuclear leucocytes. Lens—capsule intact; the central part is homogeneous. Vitreous—full of fibrinous exudates, especially below; the interstices of the network are filled with leucocytes of various kinds, but mainly polymorphonuclear. Retina—inflamed everywhere; much infiltrated with round cells, especially near the gumma; the vessels are all widely dilated, full of red corpuscles, and surrounded by dense leucocytic infiltration; rods and cones disorganised everywhere, except near posterior pole; nuclear layers retain a quasi-normal appearance. Choroid—much congested and inflamed: there is a small hæmorrhage below, just behind the gumma. Optic disc—swollen and infiltrated. Optic nerve—looks normal.

REMARKS.

The subject of gumma of the ciliary body was briefly discussed in the paper in the Transactions of the Ophthalmological Society, with a review and bibliography of the literature. There is little to add here other than to say that these cases support the conclusions arrived at there, especially as regards the microscopic identity of the so-called "papillomata" (*i.e.*, condylomata) with gummata of the ciliary body, and also as regards the absence of giant-cells in these syphilitic granulomata in this region. The diagnosis of syphilis is undoubted in Case I, though more stress is to be laid upon the rash than the history. Continental authors (*e.g.*, Ostwalt) would almost certainly class this as a condyloma, in spite of the fact that it is essentially identical microscopically with the gumma recorded in the Transactions. Whether they would class Case II with the condylomata or gummata is uncertain, and, as we have seen, quite immaterial.

A NOTE ON THE USE OF HAAB'S MAGNET.

By WILLIAM LANG.

WHEN a foreign body has been drawn forward from the vitreous chamber in the usual manner, by Haab's magnet, it may become entangled in the iris, and remain in the posterior chamber, instead of passing through the pupil to the back of the cornea, where it can drop into the bottom of the anterior chamber when the current is cut off.

When the fragment is in the anterior chamber, it can be removed through a corneal section without disturbing the iris, but as long as it is in the posterior chamber, its direct extraction has necessitated the tearing through or cutting away of a piece of the iris. To avoid this, I have used the following plan:—As soon as the foreign body, attracted by the magnet, is seen to be lifting the iris forwards, the current is cut off and the patient is placed on the operating table, which is raised to a height convenient to the surgeon. The speculum is introduced and a transverse puncture 3 or 4 mm. wide is made midway between the centre and the periphery of the cornea at a point opposite to the situation of the foreign body. If the broad needle is held with its blade in the same plane as the iris, the section can be made and the needle withdrawn without loss of aqueous. A steel spatula, made for me by Weiss, in the form of a spud, but with a rounded end, is passed between the lips of the corneal section across the anterior chamber, through the pupil and between the iris and the anterior lens capsule.

An assistant now connects the base of the spatula, by means of a few strands of soft iron wire, twisted into a rope, with Haab's magnet, which is brought close to the patient's eye; the spatula is then withdrawn with the foreign body adhering to its end. In this way Haab's magnet is made to do, in a more convenient manner, the work of the small

magnet; the iris is not bruised, torn or cut, and with reasonable care, the lense capsule is not damaged.

The flexible rope of very fine iron wire, consisting of about twenty strands 12 inches in length, is connected by means of a clamp with the magnet. If the iron wire is kept in a bottle of absolute alcohol, it remains bright and free from rust.

